Review of Test Data and Robust Summaries for

2-(2'-Hydroxy-5'-methylphenyl) benzotriazole

CAS No. 2440-22-4

CONTENTS

SUMMARY TABLE

CAS No. 2440-22-4			
PHYSICAL/CHEMICAL ELEMENTS	**DATE**	**RESULTS**	**FULFILLS REQUIREMENT**
Melting Point	1989	131 - 133 °C (measured)	Yes
Boiling Point	2000	225 °C (measured)	Yes
Vapour Pressure	2000	7.94×10^{-8} mm Hg (*)	Yes
Partition Coefficient	2000	log P = 4.2 (measured)	Yes
Water Solubility	1992	< 1 mg/L (measured)	Yes
ENVIRONMENTAL FATE AND PATHWAYS ELEMENTS			
Photodegadation	2000	For reaction with hydroxyl radical, predicted rate constant = 92.5×10^{-12} cm^3/molecule-sec predicted half-life = 1.39 h (*)	Yes
Stability in Water	2000	Low solubility makes testing impractical. EPIWIN model will not calculate for this structure.	No
Fugacity	2000	Predicted distribution using Level III fugacity model Air 3.1 % Water 4.9 % Soil 87.3 % Sediment 4.6 % Persistence = 2757 h	Yes
Biodegradation	1989	Not biodegradable (measured) 11 mg/L: 0% after 28 days 20.1 mg/L: 2% after 28 days	Yes
ECOTOXICITY ELEMENTS			
Acute Toxicity to Fish	1984	Zebra fish (Brachydanio rerio): LC_0 (96 h) > 100 mg/L (nominal) LC_{50} (96 h) > 100 mg/L (nominal)	Yes
Toxicity to Aquatic Plants		No data	No'
Acute Toxicity to Aquatic Invertebrates	1988	EC_0 (24 h) > 58 mg/L (nominal) EC_{50} (24 h) > 1000 mg/L (nominal) EC_{100} (24 h) > 1000 mg/L (nominal)	Yes

Low toxicity to algae may be extrapolated from testing with other compounds in this category.
* Estimated Value using EPIWIN Model (Syracuse Research Corporation, 2000)

SUMMARY TABLE (CONTINUED)

CAS No. 2440-22-4 HEALTH ELEMENTS	DATE	RESULTS	FULFILLS REQUIREMENT
Acute Toxicity	1978	Rat: LD_{50} (Oral) > 10,000 mg/kg	Yes
	1975	Rat: LC_{50} (Inhalation, 4 h) > 1420 mg/m^3	Yes
Genetic Toxicity in vivo	1975	Mouse: No evidence of dominant lethal effects (single gavage dose of 1000 or 3000 mg/kg). No effect on mating ratio, implantations, or embryonic death.	Yes
	1977	Chinese hamster: Nonmutagenic in somatic mutation assay (exposed by gavage 500, 1000, or 2000 mg/kg/day for 2 days)	Yes
	1981	Chinese hamster: Nomnutagenic in somatic mutation assay (exposed by gavage 500, 1000, or 2000 mg/kg/day for 2 days)	Yes
Genetic Toxicity in vitro	1982	Salmonella typhimurium: No increase in mutations with or without metabolic activation (at doses of 10, 30, 90, 270 and 810 µg/0.1 mL)	Yes
Repeated Dose Toxicity	1981	90 Day (Dog): NOEL = 1000 ppm	Yes
Reproductive Toxicity		No data	No
Developmental Toxicity/Teratogenicity:	1965	Rat: Not teratogenic NOEL = 1000 mg/kg	Yes
	1965	Mouse: Not teratogenic NOEL = 1000 mg/kg	Yes
Lifetime Carcinogenicity	1978	No evidence of carcinogenicity after 24 months exposure to the following dietary concentrations Mouse: 0, 5, 50,500 ppm Rat: 0. 100.300.1000.3000 ppm	Yes

1. MELTING POINT

Test substance:	2-(2'- Hydroxy-5'-methylphenyl) benzotriazole CAS No. 2440-22-4
Method:	From The Merck Index.'
GLP:	No
Year:	*1989*
Results:	131 – 133 °C
Remarks:	A similar melting point (128 – 132 "C) was reported by Ciba Specialty Chemicals Corp. The method of determination was not reported. The melting point was assigned a reliability code of 2g (data from handbook or collection of data).'
References:	'The Merck Index, Eleventh edition, p. 1489. [2]See listing of evaluation codes (Klimisch, H.J., et al.) p. 138

2. BOILING POINT

Test substance:	2-(2'- Hydroxy-5'-methylphenyl) benzotriazole CAS No. 2440-22-4
Method:	From Sigma-Aldrich.'
GLP:	No
Year:	2001
Results:	**225** °C
Remarks:	The boiling point was obtained from a Sigma-Aldrich MSDS, and was assigned a reliability code of 2g (data from handbook or collection of data).'
References:	'Sigma-Aldrich.com [2]See listing of evaluation codes (Klimisch, H.J., et al.) p. 138

3. VAPOR PRESSURE

Test substance:	2-(2'- Hydroxy-5'-methylphenyl) benzotriazole CAS No. 2440-22-4
Method:	Estimated by the MPBPWIN Program (v. 1.40) using the modified Grain method.[1,2]
GLP:	No
Year:	2001
Results:	7.94 x 10^{-8} mm Hg
Remarks:	A vapor pressure of 1 x 10^{-6} was reported in a MSDS from Ciba Specialty Chemicals Corp., but the method of determination was not provided. In the absence of this information, the vapor pressure was calculated using an accepted method and assigned a reliability code of 2f.[3]
References:	[1]Syracuse Research Corporation, Syracuse, NY [2]Pollution Prevention (P2) Assessment Framework, U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics (Draft), 1998 [3]See listing of evaluation codes (Klimisch, H.J., et al.) p. 138

4. PARTITION COEFFICIENT

Test substance:	2-(2'- Hydroxy-5'-methylphenyl) benzotriazole CAS No. 2440-22-4
Method:	Based on measured values (Cary 118 Spectrophotometer) at 25 degrees centigrade in water and octanol.
GLP:	*No*
Year:	**1988**
Results:	Log Pow = 4.2
Remarks:	Meets generally accepted scientific standards with acceptable restrictions. Assigned reliability code 2e.[1]
References:	H. Wyler, Report on Partition Coefficient, Ciba-Geigy Physikalische Chemie FO 6.1. September 12, 1988.

'See listing of evaluation codes (Klimisch, H.J., et al.) p. 138

5. WATER SOLUBILITY

Test substance:	2-(2'- Hydroxy-5'-methylphenyl) benzotriazole CAS No. 2440-22-4
Method:	EEC Directive 84/449 A.6
Temperature:	20 °C
GLP:	**No**
Year:	*1992*
Results:	< 1 mg/L
Remarks:	The water solubility determination was assigned a reliability code of 2b (guideline study with acceptable restrictions).[2]
References:	'Report on water solubility, Tinuvin P, Identification No. 030483.2, Ciba-Geigy Ltd., March 2, 1992.

[2] See listing of evaluation codes (Klimisch, H.J., et al.) p. 138

6. PHOTODEGRADATION

Test substance:	2-(2'- Hydroxy-5'-methylphenyl) benzotriazole CAS No. 2440-22-4
Method:	Estimated by the AOP program (v. 1.87),[1,2] which estimates rate constants and half-lives of atmospheric reactions of organic compounds with hydroxyl radicals and ozone in the atmosphere.
GLP:	No
Year:	2001
Results:	For reaction with hydroxyl radicals, the predicted half-life of the chemical was rapid. Rate constant: 92.48 x 10^{-12} cm^3/molecule-sec Half-life: 1.39 h
Remarks:	In the absence of reliable experimental data, the photodegradation was calculated using an accepted method and assigned a reliability code of 2f.[3]
References:	'Syracuse Research Corporation, Syracuse, NY *Pollution Prevention (P2) Assessment Framework, U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics (Draft), 1998 [3]See listing of evaluation codes (Klimisch, H.J., et al.) p. 138

7. STABILITY IN WATER

Test substance:	2-(2'- Hydroxy-5'-methylphenyl) benzotriazole CAS No. 2440-22-4
Method:	OECD Guideline 111
GLP:	No
Year:	2001
Results:	Due to its low solubility, we were unable to experimentally determine hydrolysis.' The HYDROWIN Program (v. 1 .67)[2,3] also was unable to evaluate this chemical structure.
Remarks:	The expert statement indicating that hydrolysis cannot be determined due to low solubility was assigned a reliability code of 2e (meets generally scientific standards, is well documented, and is acceptable for assessment).[4]
References:	'Hydrolysis of Tinuvin P as a function of pH (expert statement), Ciba Specialty Chemicals Corp., Tarrytown, NY, April 5, 2001.

'Syracuse Research Corporation, Syracuse, NY

[3]Pollution Prevention (P2) Assessment Framework, U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics (Draft), 1998.

[4]See listing of evaluation codes (Klimisch, H.J., et al.) p. 138

8. THEORETICAL DISTRIBUTION (FUGACITY CALCULATION)

Test substance:	2-(2'- Hydroxy-5'-methylphenyl) benzotriazole CAS No. 2440-22-4
Method:	Estimated by EQC Level III Fugacity Model.'
Year:	2001
GLP:	No
Results:	Distribution using EQC Level III Fugacity Model

Air	3.1 %
Water	4.9 %
Soil	87.3 %
Sediment	4.6 %

Persistence = 2757 h

Remarks: In the absence of reliable experimental data, the fugacity was calculated using an accepted method and assigned a reliability code of code of 2f.[2]

References: 'Environmental Modelling Centre, Trent University, Peterborough, Ontario, 1997

[2]See listing of evaluation codes (Klimisch, H.J., et al.) p. 138

9. BIODEGRADATION

Test substance:	2-(2'- Hydroxy-5'-methylphenyl) benzotriazole CAS No. 2440-22-4 Batch No. EN 139 879.82
Method:	OECD Guideline 301 B "Ready Biodegradability: Modified Sturm Test (CO_2 Evolution)," 1981. Bacteria was collected from activated sludge of a sewage treatment plant. The preparation was carried out according to the guideline, with the following exceptions: (1) the volume of test solution was reduced from 3 to 1.5L (2) an emulsifier, nonylphenol 10EO5PO, was added to enhance the solubility of the test material.
Test Type:	Aerobic
Concentration of the chemical:	Test chemical: 11 mg/ L and 20.1 mg/ L. Reference chemical: aniline (Merck No. 1261): 20 mg/ L
Inoculum:	Fresh sewage treatment plant sample (per guideline)
Medium:	Sewage sludge (per guideline)
GLP:	No
Year:	1989
Results:	Test chemical: 11 mg/L: 0 % after 28 days 20.1 mg/L: 2 % after 28 days Reference substance: 84.3 % after 28 days. Under the test conditions, no biodegradation was observed
Conclusion:	Substance was not biodegradable according to OECD definition.
Remarks:	This study was assigned a reliability code of 2b (guideline study with acceptable restrictions) according the criteria established by Klimisch et al (1997).[2]
Reference:	'Report on the test for ready biodegradability of Tinuvin 10047 in the modified Sturm test, Ciba-Geigy Ltd., Basle, Switzerland, February 2, 1989.

[2] See listing of evaluation codes (Klimisch, H.J., et al.) p. 138

10. ACUTE TOXICITY TO FISH

Test substance:	2-(2'- Hydroxy-5'-methylphenyl) benzotriazole CAS No. 2440-22-4 Batch No. EN 139 879.82
Method:	OECD Guideline No. 203 (Paris, 1984). This study was performed as a limit test with a concentration of 100 mg/L (nominal). Each aquarium (20 L) contained 10 fish. The exposed group consisted of 20 fish (in 2 tanks) and the control group consisted of 10 fish.
Type of test:	Static
Species:	Zebra fish (Brachydanio rerio)
Length:	*25* mm (21-28 mm)
Weight:	**0.14 g (0.10-0.19 g)**
Loading:	0.09 g/L
Exposure period:	*96 h*
Analytical monitoring:	**No**
GLP:	**No**
Year:	**1988**
Results:	LC_0 (96 h) > 100 mg/L (nominal) LC_{50} (96 h) > 100 mg/L (nominal)
Remarks:	This study was assigned a reliability code of 2b (guideline study with acceptable restrictions) according the criteria established by Klimisch *et al* (1997).[2]
Reference:	'Report on the test for acute toxicity of TK 10047 to zebra fish, Project No. 884465, Ciba-Geigy Ltd., Basel, Switzerland, December 2, 1988.

[2] See listing of evaluation codes (Klimisch, H.J., et al.) p. 138

11. TOXICITY TO AQUATIC PLANTS

Test substance: 2-(2'- Hydroxy-5'-methylphenyl) benzotriazole
CAS No. 2440-22-4

No data available

12. ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Test substance:	2-(2'- Hydroxy-5'-methylphenyl) benzotriazole CAS No. 2440-22-4 Batch No. 135146.82
Method:	OECD Guideline No. 202 (Paris 1984). A stock solution was prepared by mixing 2 g of the test chemical with 8 mg alkylphenol-polyglykol-ether, and bringing to 2 L with water. The study used 20 daphnia per concentration and control (4 replicates of 5 daphnia).
Species:	Daphnia magna Straus 1820
Type of test:	Static
Exposure period:	24 hours
Analytical monitoring:	No
GLP:	No
Year:	1988
Results:	EC_{50} (24 h) : > 1000 mg/L (nominal) EC_0 (24 h): > 58 mg/L (nominal) EC_{100} (24 h) : > 1000 mg/L (nominal)
Remarks:	The study is assigned a reliability code of 2b (guideline study with acceptable restrictions).*
Reference:	'Test for acute toxicity of Tinuvin P to Daphnia magna, Project No.: 884466, Ciba-Geigy Ltd., Basle, Switzerland, December 21, 1988.

[2]See listing of evaluation codes (Klimisch, H.J., et al.) p. 138

13. ACUTE TOXICITY

A. ORAL

Test substance:	2-(2'- Hydroxy-5'-methylphenyl) benzotriazole CAS No. 2440-22-4 Batch No. EN 40966.11
Method:	The test substancewas suspended in polyethylene glycol (PEG 400), and administered to Tif : RAIf (SPF) rats by gavage. Following single administration, animals were observed for up to 14 additional days, and monitored for clinical signs of toxicity and mortality.
Species/strain:	Tif : RAIf (SPF) rat
No. Animals/Group:	**5** lsex / dose level
Doses:	4640, 7750, 10000 mg / kg
Post dosing observation period:	**14** days
GLP:	No
Year:	1978
Results:	All treated animals showed sedation, dyspnea, curved position, and ruffled fur within 2 h after treatment. Two females in the 10,000 mg/kg group died within 7 days. All other animals recovered within 8 to 10 days following treatment. No treatment related effects were observed at necropsy. LD_{50} > 10,000 mg /kg
Remarks:	The study was assigned a reliability code of 2e, as it generally met scientific standards, was well documented, and was acceptable for assessment.'
Reference:	'Acute Oral LD_{50} In The Rat Of TK 10047, Project-no. Siss 6482, Ciba-Geigy Ltd., January 23, 1978. [2]See listing of evaluation codes (Klimisch, H.J., et al.) p. 138

B. INHALATION

Test substance:	2-(2'- Hydroxy-5'-methylphenyl) benzotriazole CAS No. 2440-22-4 Batch No. 5/4/7629/0
Method:	The test material was suspended by passing clean, dry air through a ferris wheel dust mechanism. The resulting air and dust mixture was then introduced into the exposure chamber. Five male and five female rats were exposed for 4 h at a concentration of 1420 mg/m^3 (as determined by sampling in the breathing zone). Animals were observed for 14 days after exposure, and monitored for clinical signs or toxicity and mortality. Surviving animals were sacrificed and necropsied.
Type:	Acute inhalation - dust
Species/strain:	Charles River rat
Exposure time:	4 hours
GLP:	No
Year:	*1975*
Results:	There were no effects related to exposure. No deaths occurred during the 14 day observation period, and no changes were observed during necropsy. LC_{50} (4 h) > 1420 mg/m^3
Remarks:	The study was assigned a reliability code of 2e, as it generally met scientific standards, was well documented, and was acceptable for assessment.*
Reference:	'Acute dust inhalation toxicity study with Tinuvin P Dry S-3 in Albino Rats; IBT No. 663-06501, Industrial Bio-Test Laboratories, Inc., Illinois, August 21, 1975. [2]See listing of evaluation codes (Klimisch, H.J., et al.) p. 138

14. GENETIC TOXICITY IN VIVO

A. DOMINANT LETHAL ASSAY

Test Substance:	2-(2'- Hydroxy-5'-methylphenyl) benzotriazole CAS No. 2440-22-4 Batch No. EN 2790
Method:	Male mice (20/group) were administered a single dose of the test chemical by gavage at a dose of 0, 1000, or 3000 mg/kg. Each male was placed in a cage with 2 untreated females immediately after treatment. At the end of 1 week, the females were removed and replaced by another group of 2 females. The procedure was continued to 6 consecutive weeks. The females were examined daily for successful mating, as indicated by the occurrence of a vaginal plug. The day that the vaginal plug was observed was designated as Day 0 of gestation. Females were necropsied on Day 14 of pregnancy. The number of live embryos and embryonic deaths were listed. The uteri were observed for early embryonic resorptions.
Type:	Dominant lethal assay
Species/strain:	Albino mice (NMRI derived)
Route of administration	Oral
Exposure period:	Single exposure
Doses:	1000, 3000 mg/kg
Vehicle:	Aqueous carboxymethylcellulose(0.2 mL/10 g body weight)
Control:	Concurrent. vehicle
GLP:	No
Year:	1975
Results:	No evidence of dominant lethal effects was noted. There were no differences in mating ratio, number of implantations, or embryonic deaths between controls and treated.
Remarks:	Although not conducted under GLP or OECD guidelines, this study did meet generally accepted scientific standards, was well documented, and was acceptable for assessment (reliability code 2e).[1] The findings of this study are consistent with those of other in vitro and in vivo studies for this chemical.
Reference:	'Dominant lethal study on TK 10047 mouse (Test for cytotoxic or mutagenic effects on male germinal cells), Experiment No. 327541, Ciba-Geigy Limited, Basle, Switzerland, September 11, 1975.

[2]See listing of evaluation codes (Klimisch, H.J., et al.) p. 138

B. SOMATIC MUTATION ASSAY (Interphase Nuclei)

Test substance:	2-(2'- Hydroxy-5'-methylphenyl) benzotriazole CAS No. 2440-22-4 Batch No. EN 2790
Method:	Male and female Chinese hamsters were administered the test chemical (500, 1000, or 2000 mg/kg) by gavage daily for 2 consecutive days. Twenty-four hours after the second application, animals were sacrificed and the bone marrow was harvested from the shaft of both femurs. Bone marrow cells (1000/animal) were scored for chromosomal anomalies.
Species/strain:	Chinese hamster
Sex:	Male/Female
No. Animals/group:	6 (3/sex)
Route of administration:	Oral gavage
Exposure period:	2 days
Doses:	500, 1000 and 2000 mg/kg
Vehicle:	0.5 % carboxymethylcellulose (20 mL/kg)
Controls:	Concurrent
Positive:	128 mg/kg cyclophosphamide
Negative:	Vehicle
GLP:	**No**
Year:	1976
Results:	In all groups, the percentage of cells displaying anomalies of nuclei did not differ significantly from the negative control. The positive control produced significant anomalies ($p < 0.01$).
Conclusion:	The test chemical was considered to be non-mutagenic.
Remarks:	Although not conducted under GLP or OECD guidelines, this study met generally accepted scientific standards, was well documented, and was acceptable for assessment (reliability code 2e).[2] The findings were consistent with those of other in vitro and in vivo studies for this chemical.
Reference:	'Nucleus anomaly test on somatic interphase nuclei, TK 10047, Chinese hamster (Test for mutagenic effects on bone marrow cells), Ciba-Geigy Limited, Basle, Switzerland, January 7, 1977.

[2]See listing of evaluation codes (Klimisch, H.J., et al.) p. 138

C. SOMATIC MUTATION ASSAY (Chromosomal Aberrations)

Test Material:	2-(2'- Hydroxy-5'-methylphenyl) benzotriazole CAS No. 2440-22-4, Batch No. EN 2790
Method:	Chinese hamsters in groups were administered the test chemical by gavage daily for 2 consecutive days. Animals were injected i.p. with colcemide (IO mg/kg) 2 hours after administration of the second dose and sacrificed 4 hours later. Bone marrow from 2 females and 2 males/group was harvested and analyzed for chromosomal aberrations.
Type:	Chromosomal aberration.
Species/strain:	Chinese hamsters (Cricetulus griseus)
Sex:	Male/Female
No. Animals/Group:	6 females and 4 males/treatment group) 8 females and 6 males (negative control) 10 females and 6 males (positive control)
Route of Administration:	Gavage
Exposure period:	2 days
Doses:	500, 1000 and 2000 mg/kg
Controls:	Concurrent Positive: cyclophosphamide (64 mg/kg) Negative: vehicle
Vehicle:	2% sodium carboxymethylcellulose (20 mL/kg)
GLP:	*No*
Year:	*1981*
Results:	The chromosome displays from the animals treated with the test chemical showed no aberrations. In the negative control group, two metaphase figures showing aberrations were observed. A significant increase in aberrations was observed among the positive controls
Conclusion:	Not mutagenic.
Remarks:	Although not conducted under GLP or OECD guidelines, this study did meet generally accepted scientific standards, was well documented, and was acceptable for assessment (reliability code 2e).[2] The findings of this study were consistent with those of other in vitro and in vivo studies for this chemical.

Reference:

‘Chromosome studies in somatic cells, TK 10047, Chinese hamster, Test for mutagenic effects on bone marrow cells. Experiment No. 40270576, Ciba-Geigy Limited, Basle, Switzerland, August 2.5, 1981.

[2]See listing of evaluation codes (Klimisch, H.J., et al.) p. 138

15. GENETIC TOXICITY IN VITRO

Test substance:	2-(2'- Hydroxy-5'-methylphenyl) benzotriazole CAS No. 2440-22-4 Batch No.: EN 3915
Method:	This study was not conducted under OECD guidelines, but was conducted using the methods described by Ames et a/ (1973, 1975).[2-4] The material was tested for mutagenic effects on histidine - auxotrophic mutants of Salmonella typhimurium (TA 98, TA 100, TA 1535 and TA 1537). The investigations were performed with the following concentrations of the trial substance with and without microsomal activation: 10, 30, 90, 270 and 810 µg/ 0.1 ml.
Type:	Bacterial mutagenicity
System of testing:	Salmonella typhimurium TA 98, 100, 1535, 1537
GLP:	No
Year:	1979
Results:	The test chemical did not increase mutations with or without metabolic activation.
Conclusion:	Not mutagenic
Remarks:	This study was assigned reliability code of 2e (met generally accepted scientific standards, was well documented, and was acceptable for assessment).[5]
References:	'Salmonella/ mammalian - microsome mutagenicity test with TK 10047. (Test for mutagenic properties in bacteria), Ciba-Geigy Ltd, Basel, Switzerland, January 25, 1979. [2]Ames, B.N., Lee, F.D., and Durston, W.E., "An improved bacterial test system for the detection and classification of mutagens and carcinogens, Proc. Natl. Acad. Sci. USA, 70, 782-786, 1973. [3]Ames, B.N., Durston, W.E., Yamasaki, E., and Lee, F.D., "Carcinogens are mutagens: a simple test system combining liver homogenates for activation and bacteria for detection," Proc. Natl. Acad. Sci. USA, 70, 2281-2285, 1973. [4]Ames, B.N., McCann, J., and Yamasaki, E., "Methods for detecting carcinogens and mutagens with the Salmonella/mammalian-microsome mutagenicity test, Mutat. Res., 31, 347-364, 1975. [5]See listing of evaluation codes (Klimisch, H.J., et al.) p. 138

16. REPEATED DOSE TOXICITY

A. 90 - Day Toxicity study on dogs:

Test substance:	2-(2'- Hydroxy-5'-methylphenyl) benzotriazole CAS No. 2440-22-4
Method:	Although this study was not formally conducted under OECD guidelines, the method paralleled OECD Guideline 409 "Subchronic Oral Toxicity – Non-Rodent: 90-Day Study." The study was monitored for compliance with Ciba's internal QA guidelines. In this study, each group was administered the test chemical in the diet at the specified concentration for 13 weeks. The test chemical was dissolved in PEG 400, and mixed with dog food. After the 13 week period, 1 animal/sex/dose group was fed the control diet for a period of 1 month to test for recovery.
Species/strain:	Beagle dog
Age:	31 - 34 weeks
Initial weight:	Male: 8.1 kg -12.4 kg, Female: 6.4 kg - 10.7 kg
No. of animals/group:	G/sex/group
Route of administration:	Dietary
Exposure period:	91 days (13 weeks)
Frequency of treatment:	Daily
Dose:	0, 1000, 3000, and 10,000 ppm in food
GLP:	**No**
Year:	1981
Results:	NOEL = 1000 ppm (Males: 31.75 mg/kg; Females: 34.6 mg/kg) No mortality or symptoms of local and/or systemic toxicity was observed. Decreased food consumption and body weight gain for the 10,000 ppm group were noted. There were no effects of treatment on opthalmology or auditory perception. Increased alanine aminotransferase in the 3000 ppm and 10,000 ppm groups and increased gamma-glutamyl transpeptidase in the 10,000 ppm group were reported. One female animal from the 10,000 ppm was emaciated. There were no gross or histopathological changes related to treatment.
Remarks:	This study was assigned a reliability code of 2c (comparable to guideline study with acceptable restrictions) according to the guidelines described by Klimisch et *al* (1997).[2]

Reference: 'Final report, TK 10047 - three-month toxicity study on dogs, Project No. 790858, Ciba - Geigy Limited, Basel, Switzerland, November 25, 1981.

[2]See listing of evaluation codes (Klimisch, H.J., et al.) p. 138

B. LIFETIME CARCINOGENICITY IN MICE

Test substance: 2-(2'- Hydroxy-5'-methylphenyl) benzotriazole
CAS No. 2440-22-4
Batch No.: EN 71000

Method:	Although this study was not conducted under OECD guidelines, the study was monitored for compliance with Ciba's internal QA guidelines. The experiment was carried out under specified pathogen free (SPF) standard laboratory conditions. The animals were housed in groups of 5 in Macrolon cages type 3 with standardized granulated soft wood bedding. Temperature was maintained at 22 ± 2 °C with relative humidity of 55 ± 10 % and 10 hours light/day. Tap water of drinking water quality was provided ad libitum. Pelleted, certified standard diet (Nafag No. 89) was provided ad libitum. The test compound was administered daily in the diet for 24 months. Neither insecticides nor chemicals were applied in the animals room with the exception of disinfectant: Fungitex SB (Prod. Nr. 30071, CIBA-GEIGY LTD.).
Species/strain:	Mice Tif: MAGf (SPF)* * F3 -hybrid of (imbred NMRI = MAG Tif) x NIH/NMRI Tif
No. of animals:	50 Males and 50 Female/ group (total 400)
Initial mean group body weight: (week - 1)	21.7 - 22.3 g (males) 20.4 - 21 .O g (females)
Initial Age:	Approx. 4 weeks
Method of randomization:	In order to set up a fully randomized experiment, the animals were assigned to the different groups by means of random numbers generated by the IBM computer of CIBA-GEIGY LTD., Basle/Switzerland.
Route of administration:	Diet
Duration of the test:	24 months
Dose:	0, 5, 50, 500 ppm
Year:	*1981*
GLP:	No, but quality assurance inspections were performed.
Summary And Assessment:	A total of 400 MAGf (SPF) mice (50 males and 50 females per dose group) was used. The test article was administered in the diet for 24 months at dosages of 0, 5, 50 and 500 ppm. The results of the study may be summarized as follows: The mean body weight gain of all treated male and female groups was similar to the controls. The mean food consumption of all treated male and female groups was similar to that of the respective controls. The mean food conversion of all treated groups was similar to the controls. Median survival time and mortality distribution of treated groups was

similar to the controls.

No clinical symptoms and no signs of local and/or systemic toxicity were observed.

Apart from a marked decrease of the liver weight in the male 50 ppm group and a slight increase in adrenal weights in treated female groups, analysis of organ weights and ratios revealed no consistent effects. Above variations are common in aged animals and considered to be unrelated to the treatment.

Neither gross nor microscopical changes in the organs and tissues related to the treatment were noted. Numerous benign and malignant tumors were observed in both control and treated mice. Frequency and type of the neoplasms occurring in these animals were not influenced by the treatment.

Other gross and histopathological lesions and changes seen in both control and test animals and described as developmental, degenerative or inflammatory in origin are attributed to the naturally occurring diseases which are common in aged mice of this breeding colony.

It can be inferred from the observations made during the above study that the test substance when administered to mice daily in the diet over a period of 24 months at dietary levels of 5, 50 and 500 ppm corresponding to a mean daily intake of 0.8, 6.5 and 64 mg/kg bw. in male and 0.8, 6.7 and 62 mg/kg bw. in female animals, respectively did not produce inflammatory, degenerative, proliferative or neoplastic lesions.

Statistical Analysis:

For each time point and parameter a uni-variate statistical analysis was conducted. Due to the routine manner of the analysis system, parameter free methods were applied. Each treated group was compared to the control group in respect of dispersion and displacement[3]. In addition a trend test[4] was applied considering all groups.

Survival analysis was performed by the generalized Wilcoxon Test[5] (Breslow 1970) and the generalized Savage Test[6] (Mantel-Cox 1966.) The Mantel-Cox and Breslow Tests differ in the way they weight observations. The Breslow Test gives greater weight to early observations, and is less sensitive to late events which occur when few animals on the study remain alive. Both tests are valid in large samples whether the censoring patterns (moribund sacrifice of interim sacrifice) are equal or unequal.

Statistical analysis is performed to draw attention to distinct values. A statistically significant difference between two values does not necessarily imply biological relevance of that deviation and is not conclusive for a treatment related effect.

Remarks

This study was assigned a reliability code of 2 (Valid with restriction) according to the guidelines described by Klimisch et *al* (1997).[2]

Reference:

'Final Report TK 10047 - Lifetime Carcinogenicity Study in Mice, Project No. 784334. Ciba Geigy Limited, Basel, Switzerland. Prof. Dr. Med. R. Hess, 08/17/81.

[2]See listing of evaluation codes (Klimisch, H.J., et al.) p. 138

[3]Lepage Y., Biometrika (1971) 58: pp. 213-217

[4]Jonckheere H.R., Biometrika (1954) 41: pp. 133-145

[5]Breslow N., Biometrika (1970) 57: pp. 579-594

'Mantel N., Cancer Chemotherapy Reports (1966) 50: pp. 163-170

C. LONG TERM FEEDING TO RATS:

Test substance: 2-(2'- Hydroxy-5'-methylphenyl) benzotriazole
CAS No. 2440-22-4

Method: Five hundred, 25 ± 1 days old, CFY rats, a hysterectomy-derived strain of Sprague-Dawley origin, were obtained for allocation to the following five treatment groups:

	Group and treatment	No. of rats	
		males	females
1	Control (untreated diet)	50	50
2	100 ppm	50	50
3	300 ppm	50	50
4	1000 ppm	50	50
5	3000 ppm	50	50

Throughout the investigation, the rats were housed five to a cage (unless the number was reduced by mortality) in suspended metal cages fitted with wire-mesh floors. Animal-room temperature and relative humidity were controlled at 21 ± 2°C and 55 ± 5% respectively; lighting was controlled to give 12 hours of light (8 a.m. to 8 p.m.) and 12 hours of darkness per 24 hours. All rats had free access to tap water and to quantities of powdered laboratory rat food, Spratt's Laboratory Animals Diet No. 2. For the treated groups, the test substance was incorporated in this diet.

Species/strain: Rats (CFY strain)

Age: 25 ± 1 days old

No. of animals/group: 50 males and 50 females/group

Route of administration: Dietary

Total duration of dietary intake: 104 weeks

Frequency of treatment: Daily

Dose: 100 ppm (4-6 mg/kg bodyweight/day)
300 ppm (14-17 mg/kg bodyweight/day)
1000 ppm (47-58 mg/kg bodyweight/day)
3000 ppm (142-l 69 mg/kg bodyweight/day)

GLP: **No**

Year: *1975*

Results:

Reactions to treatment at the various dietary levels are summarized as follows:

3000 ppm

Slightly decreased bodyweight gain among males during the second year of treatment ($P<0.05$) and slightly reduced food intake among females during the period 53 to 80 weeks of treatment ($P<0.05$).

1000,300 or 100 ppm

The performance of rats treated at these levels was comparable with that of the controls.

Mortality

A marginally lower survival rate was recorded during the final 26 weeks of treatment among males in the 3000 ppm group although the difference from the control male group survival rate did not attain a level of significance. Survival rates among other treated rats was similar to that of the controls.

Bodyweight

Among male rats at 3000 ppm, an inferior mean bodyweight gain was recorded during the last 52 weeks of treatment in comparison with that of the control group ($P<0.05$).

Body-weight gains among other treated rats were not affected by treatment.

Food Consumption

Food intake of rats treated with 100 or 300 ppm and males treated with 1000 ppm remained comparable with that of the controls throughout the study.

Hematoloav

Although at week 13, a statistically significant reduction in red blood cell count, with the consequent elevation of the mean cell volume, was observed in male rats receiving 3000 ppm, the values were within the “normal” range for the strain of rat employed. The differences were therefore, not considered to be of biological significance.

Blood chemistry

Among rats treated with 3000 ppm, there was a marginal reduction in urea nitrogen recorded among females at week 13, and a marginal increase among males at week 26, females at week 78 and males at week 102. With the exception of the values recorded for males treated with 3000 ppm, all values for urea nitrogen recorded during the study were within the “normal” limits for the strain of rat employed.

Macroscopic Pathology

The macroscopic pathology among rats dying during the course of the study showed no relation to treatment.

Oraan Weioht Analysis.

Organ weight analysis performed on rats killed after 104 weeks of treatment revealed slightly heavier thyroid/parathyroid weights among treated animals, which only attained a level of statistical significance among males treated with 1000 ppm and females treated with 1000 or 3000 ppm when related to bodyvveight. As the values obtained for treated rats were within the normal range for CFY rats, the differences were considered to have arisen fortuitously.

General histopathology of rats killed after 104 weeks of treatment showed no morphological abnormalities and variations from normal.

Total tumor incidence

There were slightly more tumor-bearing rats among females at 300 or 1000 ppm, killed after 104 weeks of treatment, compared to controls, although these differences did not attain a level of statistical significance. The incidence of tumor-bearing rats in other treated groups was comparable with that of the controls.

The distribution of tumors of the endocrine glands showed no treatment-related disturbance. The incidence recorded was within the normal limits previously recorded within our laboratories for the CFY rat.

The administration of the test substance was not associated with any evidence of an effect on the spontaneous tumor.

Conclusion:

Based on the above findings it was concluded that 1000 ppm (47-58 mg/kg bodyweight/day) was the no-effect level.

The marginally lower bodyweight shown by some males on 3000 ppm and the slightly lower food consumption of some females on the same dose recorded during the second year of the study is difficult to assess. Therefore, the possibility that 3000 ppm (142-l 69 mg/kg bodyweight/day) was also without effect must be considered.

Remarks:

This study was assigned a reliability code of 2 (valid with restrictions) according to the guidelines described by Klimisch et *al* (1997).[2]

Reference:

'Long - Term Feeding of TK 10047 to Rats (Final Report 0 -104 weeks), Ciba - Geigy Limited, Basel, Switzerland, March 20, 1975.

[2]See listing of evaluation codes (Klimisch, H.J., et al.) p. 138

17. REPRODUCTIVE TOXICITY

Test substance: 2-(2'- Hydroxy-5'-methylphenyl) benzotriazole
CAS No. 2440-22-4

No data found

18. DEVELOPMENTAL TOXICITY/ TERATOGENICITY

A. TERATOGENICITY IN RATS

Test substance:	2-(2'- Hydroxy-5'-methylphenyl) benzotriazole CAS No. 2440-22-4 Batch : EN 2970
Method:	Although this study was not formally carried out under OECD guidelines, the methods closely paralleled OECD Guideline 414 "Teratogenicity," adopted May 12, 1981. The compound was administered by oral gavage on Days 6 through 15 of gestation. During the treatment, general condition, weight gain, food consumption and symptomology were checked daily. Dams were killed, and fetuses removed by Cesarean section on Day 21 of gestation. The examinations were carried out in accordance with the World Health Organization recommendations (WHO, 1967) and the technique described by Wilson, 1965.[2,3]
Species/strain:	Sprague-Dawley rat
Sex:	Female
Route of administration:	Gavage
Duration of the test:	0 days
Exposure period:	Days 6 through 15 of gestation
Frequency of treatment:	Daily
Doses:	150,500, 1000 mg/kg
Vehicle:	2% aqueous carboxymethylcellulose(1 mL/1 00g body weight)
Control group:	Concurrent vehicle
GLP:	*No*
Year:	*1975*
Results:	NOEL = 1000 mg/kg Maternal general toxicity: No reaction to treatment was noted. Pregnancy/litter data: The rates on implantation and embryotoxicity were not significantly affected by treatment. Fetal data: No teratogenic effects were noted.

Conclusion: The material was considered nonteratogenic under the test conditions.

Remarks: This study was assigned a reliability code of 2c (comparable to guideline study with acceptable restrictions).[4] An additional teratogenicity study was conducted in mice which supports the conclusion of this study.

References: '"Reproduction Study – TK 10047, Rat, Segment II (Test for Teratogenic or Embryotoxic Effects)', Test No. 227525. Ciba Geigy Limited, Basel, Switzerland. Dr. H. Fritz, 06/19/75.

'World Health Organization Technical Report Service 364, 1967

[3]Wilson, J.G., in: Teratoloov, Principles and Techniuues; J.G. Wilson and J. Warkany eds., The University of Chicago Press, Chicago, 1965, pp. 262-277.

[4]See listing of evaluation codes (Klimisch, H.J., et al.) p. 138

B. TERATOGENICITY IN MICE

Test substance:	2-(2'- Hydroxy-5'-methylphenyl) benzotriazole CAS No. 2440-22-4 Batch : EN 2790
Method:	Although this study was not formally carried out under OECD guidelines, the methods closely paralleled those described in OECD Guideline 414 "Teratogenicity," adopted May 12, 1981. The compound was administered by oral gavage on Days 6 through 15 of gestation. During the treatment, general condition, weight gain, food consumption and symptomology were checked daily. Dams were killed, and fetuses were removed by Cesarean section on Day 18 of gestation. The examinations were carried out in accordance with the World Health Organization (WHO) recommendations (WHO, 1975) and the technique described by Wilson, 1965.[2,3]
Species/strain:	Albino mouse (NMRI derived)
Sex:	Female
Route of administration:	Gavage
Duration of the test:	10 Days
Exposure period:	Days 6 through 15 of gestation
Frequency of treatment:	Daily
Doses:	150, 500, 1000 mg/kg
Vehicle:	2% aqueous carboxymethylcellulose (0.1 mL/10 g body weight)
Control group:	Concurrent vehicle
GLP:	No
Year:	**1975**
Results	NOEL = 1000 mg/kg Maternal general toxicity: No reaction to treatment was noted Pregnancy/litter data: The rates on implantation and embryotoxicity were not significantly affected by treatment. Fetal data: No teratogenic effects were noted.
Remarks:	This study was assigned a reliability code of 2c (comparable to guideline study with acceptable restrictions).[4]

References:

'"Reproduction Study – TK 10047, Mouse, Segment II (Test for Teratogenic or Embryotoxic Effects)', Test No. 327535. Ciba Geigy Limited, Basel, Switzerland. Dr. H. Fritz, 08/28/75.

'World Health Organization Technical Report Service 563, 1975

[3]Wilson, J.G., in: Teratoloav, Principles and Techniques; J.G. Wilson and J. Warkany eds., The University of Chicago Press, Chicago and London, 1965, pp. 262-277.

[4]See listing of evaluation codes (Klimisch, H.J., et al.) p. 138

Review of Test Data and Robust Summaries for

2-(2'-hydroxy-5'-octylphenyl) benzotriazole

CAS No. 3147-75-9

CONTENTS

SUMMARY TABLE

CAS No. 3147-75-9			
PHYSICAL/CHEMICAL ELEMENTS	**DATE**	**RESULTS**	**FULFILLS REQUIREMENT**
Melting Point	2000	106 - 108 °C (measured)	Yes
Boiling Point		not applicable	Yes
Vapour Pressure	2001	1.1 x 10^{-9} mm Hg (*)	Yes
Partition Coefficient	1984	Log Kow = 6.21 (*)	Yes
Water Solubility		< 1 mg/ L (measured)	Yes
Water Solubility	2000	0 . 1 6 7 8 mg/L (*)	Yes
ENVIRONMENTAL FATE AND PATHWAYS ELEMENTS			
Photodegradation	2000	For reaction with hydroxyl radical, predicted rate constant = 3 1.95 x 10^{-12} cm^3/molecule-sec predicted half-life = 4.017 h (*)	Yes
Stability in Water	2000	This program cannot estimate a hydrolysis rate for this type of structure.	Data Required
Fugacity (*)	2000	Predicted distribution using Level III fugacity model Air: 4.01x 10^{-5}% Water:3.47% Soil:44.6% Sediment: 5 1.9%	Yes
Biodegradation	2000	Not readily biodegradable (measured)	Yes
ECOTOXICITY ELEMENTS			
Acute Toxicity to Fish	1989	Zebra fish (Brachydanio rerio): LC_{50} (96 h) > 100 mg/L	Yes
Toxicity to Aquatic Plants	1993	Scenedesmus subspicatus EC_{50} (72 h) > 100 mg/L NOEC (O-72 h) > 100 mg/L	Yes
Acute Toxicity to Aquatic Invertebrates	1984	Daphnia magna straus 1820 EC_0 (24 h): 0.10 mg/L EC_{50} (24 h): 15 mg/L	Yes

* Estimated Value using EPIWIN Model (Syracuse Research Corporation, 2000)

SUMMARY TABLE (CONTINUED)

CAS No. 3147-75-9 HEALTH ELEMENTS	**DATE**	**RESULTS**	**FULFILLS REQUIREMENT**
Acute Toxicity	1968	Rat: LD_{50} (Oral) > 1000 mg/kg	Yes
Genetic Toxicity in vivo		No data available	No
Genetic Toxicity in vitro	1991	Not mutagenic	
Repeated Dose Toxicity	1968	Rats, 30-day, Dietary NOAEL = 5658 mg/ kg.	Yes
Reproductive Toxicity		No data available	No
Developmental Toxicity/Teratogenicity		No data available	No

1. MELTING POINT

Test substance:	2-(2'-hydroxy-5'-octylphenyl) benzotriazole CAS# 3 147-75-9
Method:	From Sigma-Adrich.'
GLP:	**No**
Year:	2001
Results:	106 - 108 °C
Remarks:	The melting point was obtained from a Sigma-Aldrich MSDS, and assigned a reliability code of 2g (data from handbook or collection of data).[2] The MSDS from Ciba Specialty Chemical Corp. reported a similar melting point range of 103 to 105 °C.
References:	'Sigma-Aldrich.com

[2] See listing of evaluation codes (Klimisch, H.J., et al.) p. 138

2. BOILING POINT

Test substance:	2-(2'-hydroxy-5'-octylphenyl) benzotriazole CAS# 3 147-75-g
Method:	Not applicable, material is solid.

3. VAPOR PRESSURE

Test Substance:	2-(2'-hydroxy-5'-octylphenyl) benzotriazole CAS# 3147-75-9
Method:	Estimated by the MPBPWIN Program (v.1.40)[1], using the Modified Grain Method.
GLP:	No
Year:	***2001***
Results:	1.1×10^{-9} mm Hg @ 25 C
Remark:	The vapor pressure calculated by an accepted method is assigned a reliability code of 2f according to the criteria established by Klimisch et *al.* ***(1997)'.***
References:	'Syracuse Research Corporation, Syracuse, NY Pollution Prevention (P2) Assessment Framework, U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics (Draft), 1998 [2] See listing of evaluation codes (Klimisch, H.J., et al.) p. 138

4. PARTITION COEFFICIENT

Test Substance:	2-(2'-hydroxy-5'-octylphenyl) benzotriazole CAS# 3 147-75-9
Method:	Estimated by the KowWin Program (v.1.66)[1]
GLP:	No
Year:	2001
Results:	Log Kow = 6.21
Remark:	The partition coefficient calculated by an accepted method is assigned a reliability code of 2f according to the criteria established by Klimisch et al. (1997)[2].
References:	'Syracuse Research Corporation, Syracuse, NY Pollution Prevention (P2) Assessment Framework, U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics (Draft), 1998 [2] See listing of evaluation codes (Klimisch, H.J., et al.) p. 138

5. WATER SOLUBILITY

Test Substance:	2-(2'-hydroxy-5'-octylphenyl) benzotriazole CAS# 3 147-75-9
Method:	The water solubility was estimated using WSKOW (v. 1.37)'
GLP:	No
Year:	2001
Results:	0.1678 mg/L @ 25°C
Remark:	The water solubility calculated was assigned a reliability code of 2f according to the criteria established by Klimisch et al. (1997).[2]
References:	'Syracuse Research Corporation, Syracuse, NY Pollution Prevention (P2) Assessment Framework, U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics (Draft), 1998

[2] See listing of evaluation codes (Klimisch, H.J., et al.) p. 138

6. PHOTODEGRADATION

Test Substance:	2-(2'-hydroxy-5'-octylphenyl) benzotriazole CAS# 3147-75-g
Method:	Estimated by the AOP program (v1.90)[1], which estimates rate constants and half-lives of atmospheric reactions of organic compounds with hydroxyl radicals and ozone in the atmosphere.
GLP:	No
Year:	2001
Results:	For reaction with hydroxyl radicals, the predicted half-life of the chemical is relatively rapid. Rate constant: 31.95 x 10^{-12} cm^3/molecule-sec Half-life: 4.017 hours
Remark:	The photodegradation rate calculated by an accepted method is assigned a reliability code of 2f according to the criteria established by Klimisch et al. (1997).[2]
References:	'Syracuse Research Corporation, Syracuse, NY Pollution Prevention (P2) Assessment Framework, U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics (Draft), 1998 [2] See listing of evaluation codes (Klimisch, H.J., et al.) p. 138

7. HYDROLYSIS

Test Substance:	2-(2'-hydroxy-5'-octylphenyl) benzotriazole CAS# 3147-75-g
Method:	Estimated by the HYDROWIN program (v1.67)[1].
GLP:	No
Year:	2001
Results:	Unable to estimate hydrolysis for this structure.
Remark:	
Reference:	'Syracuse Research Corporation, Syracuse, NY Pollution Prevention (P2) Assessment Framework, U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics (Draft), 1998

8. TRANSPORT (FUGACITY)

Test Substance:	2-(2'-hydroxy-5'-octylphenyl) benzotriazole CAS# 3 147-75-9
Method:	Estimated by the Level III Fugacity Model (Full-Output)
GLP:	No
Year:	2001
Results:	Distribution using Level III Fugacity Model:

Air:	4.01x 10^{-5}%
Water:	3.47%
Soil:	44.6%
Sediment:	51.9%

Remark: The fugacity calculated by an accepted method is assigned a reliability code of 2f according to the criteria established by Klimisch et al. (1997).[2]

References: 'Syracuse Research Corporation, Syracuse, NY

Pollution Prevention (P2) Assessment Framework, U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics (Draft), 1998

[2] See listing of evaluation codes (Klimisch, H.J., et al.) p. 138

9. BIODEGRADATION

Test Substance:	2-(2'-hydroxy-5'-octylphenyl) benzotriazole CAS# 3147-75-9
Method:	The protocol generally followed OECD Guideline 301 B (May 1981), Ready Biodegradability: Modified Sturm Test. The only deviation from the test guideline is the volume of the test solution was reduced from 3.0 L to 1.5 L. Due to the poor solubility of the test substance in water, an emulsifier was used to achieve a better distribution in the medium. The test substance was added to the medium and homogenized with Nonylphenol 10EO5PO.
Test System:	Bacteria collected from a sewage treatment plant.
Duration:	28 days
Temperature:	22 ± 2^0 C
Reference Substance:	Aniline MERCK No.:1261
Concentrations:	Reference substance: 20 mg/ L Test substance: 10.2 mg/ L, and 21.5 mg/ L.
Year:	**1989**
Results:	The biodegradation was calculated as: Reference substance: 20 mg/L - 80% in 28 days Test substance: 10.2 mg/L - 0% in 28 days 21.5 mg/L - 1% in 28 days
Conclusion:	Substance is not biodegradable according to OECD definition.
Remarks:	This study is assigned a reliability code of 1 b as it was conducted under OECD Guidelines.[2]
Reference:	Report on the Test for Ready Biodegradability of Tinuvin 329 In The Modified Sturm Test (OECD-Guideline No. 301 B, Paris 1981); (1989), Dr. A. De Morsier, Dr. U. Bader; Ciba-Geigy Ltd. Basle, Switzerland.

[2] See listing of evaluation codes (Klimisch, H.J., et al.) p. 138

10. ACUTE TOXICITY TO FISH

Test Substance:	2-(2'-hydroxy-5'-octylphenyl) benzotriazole CAS# 3147-75-9
Method:	The test was conducted under OECD Guideline No. 203 (Paris 1984). Glass aquaria of 20 liters filled with 15 liters of dechlorinated tap water (carbon filter). Hardness of water is 179 mg $CaCO_3$ / L. The temperature was maintained at 23 ± 1 °C, and lighted for 16 hours daily with florescent light. Oxygen, pH and temperature were measured daily. No stock solution was prepared. The test substance and 4 mg/ L alkylphenol-polyglykol-ether were added directly to the water in the tanks. Ten fish per concentration were used.
Type of Test:	Static
Species	Zebra Fish (Brachydanio rerio)
Number of fishes:	IO fish per concentration and control IO fish per aquarium
Length:	30 mm (27-32 mm)
Weight:	0.24 g (0.19 - 0.32 g)
Loading:	0.16 g/L
Feeding:	None
Temperature:	23 ± 1°C
Exposure period:	96 hours
Test Concentration:	IO, 18, 32, 58, 100 mg/L (nominal)
Controls:	Blank: Water Vehicle: 4 mg alkylphenol-polyglykol-ether per liter water
Analytical monitoring:	No
Year:	1989
Results:	There were no mortalities in control or treated groups. LC_{50} (24 h): > 100 mg/L LC_{50} (48 h): > 100 mg/L LC_{50} (72 h): > 100 mg/L LC_{50} (96 h): > 100 mg/L

Table 1 : Symptoms observed at different test concentrations

Nominal Conc. Mg/L	Swimming behavior				Loss of equilibrium				Respiratory function				Exophtalmus				Pigmentation			
	24	48	72	96	24	48	72	96	24	48	72	96	24	48	72	96	24	48	72	96
Blank	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Vehicle	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
10	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
18	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
32	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
58	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
100	0	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Effect:
0 = Normal
1 = Slight
2 = Moderate
3 = Severe

Remarks: This study is assigned a reliability code of 2b (guideline study with acceptable restrictions) according the criteria established by Klimisch et *al* (1997), as it was conducted under OECD Guidelines.

Reference: Report On The Test For Acute Toxicity Of Tinuvin 329 To Zebra Fish; Sept 13, 1989, Project No.: 894204; Drs H. Rufli, A. De Morsier; Ciba-Geigy Ltd., Basle, Switzerland.

11. ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Test Substance:	2-(2'-hydroxy-5'-octylphenyl) benzotriazole CAS# 3 147-75-9
Method:	OECD Guideline No. 202 (Paris 1984). Reconstituted water was prepared by dissolving 65 mg $NaHCO_3$, 274 mg $CaCl_2$ (2 H_2O), 123 mg $MgSO_4$ (7 H_2O), 6 mg KCI in 1 liter of bidistilled water. Total hardness was 240 mg $CaCO_3$/L. The water was aerated with clean air for at least 24 hour before use. The temperature was maintained at 23 ± 1°C, and lighted for 16 hours daily with fluorescent light. Oxygen, pH and temperature were measured daily. Twenty daphnia/conc and control were used. The test substance appeared homogeneously distributed. The EC50 values were calculated according to the maximum likelihood method, logit model (McCullagh, P., Nelder, J.A., 1983: Generalized linear models, Chapman & Hall, London)
Species:	Daphnia magna Straus 1820
Exposure period:	24 hours
Number of Daphnia:	20 daphnia per concentration and control 4 replicates of 5 daphnia each
Test Concentration:	0.058, 0.10, 0.18, 0.32, 0.58, 1.0, 1.8, 3.2, 5.8, 10, 18 mg/L
Controls:	Blank: Water. Vehicle: 0.36 mg sorbitan-fatty acid ester polyglykol ether per liter water in the concentration used for the highest test concentration.
Analytical monitoring:	Yes.
GLP:	No.
Year:	1989
Results:	EC_{50} (24 h) calculated : 15 mg/L EC_{50} (24h) graphically determined : 16 mg/L EC_0 (24h) in test : 0.10 mg/L EC_{100} (24h) : > 18 mg/L Controls: Immobilization in blank 0 % Immobilization in vehicle 0 % Values are based on nominal concentrations

Remarks:	The study is assigned a reliability code of 2b: Guideline study with acceptable restrictions according the criteria established by Klimisch et *a/ (1997).*
Reference:	Report On The Test For Acute Toxicity of Tinuvin 329 To Daphnia Magna; Oct., 1989, Project No.: 894202; Drs. A. de Morsier, H. Rufli,; CIBA-GEIGY Ltd., Basel, Switzerland.

12. TOXICITY TO AQUATIC PLANTS

Test substance:	2-(2'-hydroxy-5'-octylphenyl) benzotriazole CAS# 3 147-75-9
Method:	The protocol followed 87/302/EEC page 89-94 Algal growth inhibition test. Tests were conducted in 100 mL Erlenmeyer flasks, stoppered with aluminium caps containing 50 mL of test solution per flask. Each test level was prepared in 3 replicates and control in 6. Temperature was maintained at 22 ± 2°C with continuous illumination. pH was measured at 0 and 72 hour exposure. Two g test substance and 18 g of a 0.4 % alcyl-phenol-polyglycol-ether solution (Arkopal) were mixed together by means of a marble-mill for about 24 hours. One mL of this blend were mixed and made up to 100 mL with water achieving a concentration of 100 mg/ L. The test substance was homogeneously distributed in the test vessels at all test times and test concentrations except at test concentrations 3.7, 11, 33 and 100 mg/ L where small amounts of the test substance were visible on the surface of the test water after 72 hours of exposure. Cell densities were measured at 24, 48, and 72 hours exposure. The EC50 values were calculated according to the maximun likelihood method, probit model (Mc Cullagh, P., Nelder, J.A., 1983: Generalized linear models, Chapman & Hall, London)
Species:	Green Algae *(Scenedesmus subspicatus)*
Exposure period:	72 h
Initial Cell Density:	10^4 cells/mL
Test Concentrations:	Nominal : 1.23, 3.7, 11, 33 and 100 mg/L
Controls:	Blank: water Vehicle: 3.6 mg Arkopal/ L (Arkopal = alcyl-phenol-polyglycol-ether)
Analytical monitoring:	**No** Testing based on nominal concentrations.
GLP:	**No.**
Year:	**1993**
Results:	EC_{50} (0 – 72 h) > 100 mg/L NOEC(O-72h): lOOmg/L Values based on nominal concentrations.

TABLE 1

CELL DENSITIES AFTER 24, 48, 72 HOUR EXPOSURE

Initial cell density: 10500 cells/ ml

CONC. NOMINAL (mg/ L)	MEAN DENSITY CELLS/ ML * 10000		
	24 HOUR	48 HOUR	72 HOUR
Blank	4.0	35.9	209.8
Vehicle	4.2	26.0	151.5
1.23	5.2	44.7	218.3
3.7	4.6	44.0	214.2
11	5.0	53.3	228.3
33	2.1	41.9	196.3
100	3.6	43.8	186.7

TABLE 2

INHIBITION

CONC. NOMINAL (mg/ L)	AREA UNDER GROWTH CURVES (A) * 10000						MEAN A	INHIBITION * IA O-72 HOUR %
	1	2	3	4	5	6		
Blank	3465	3663	3341	3382	3322	3295	3411	0.0
Vehicle	2500	2468	2468				2479	27.3
1.23	3676	3773	3812				3754	0.0
3.7	3535	3854	3633				3674	0.0
11	3943	3856	4431				4077	0.0
33	3465	3256	3321				3347	1.9
100	3347	3742	2853				3314	2.8

Remarks: This study is assigned a reliability code of 2C (comparable to guideline study with acceptable restrictions) according the criteria established by Klimisch et *al* (1997).

Reference: Report on the growth inhibition test of Tinuvin 329 to green algae (*Scenedesmus subspicatus)*;Jan., 20, 1993; Dr. R. Grade, CIBA-GEIGY Ltd., Basel, Switzerland.

13. ACUTE ORAL TOXICITY'

Test Substance:	2-(2'-hydroxy-5'-octylphenyl) benzotriazole, CAS# 3147-75-9
Method:	Animals were housed at room temperature, 5/cage, and fasted 24 hours before dosing. Test material was dosed as in 10% aqueous mixture. Animals were dosed by oral gavage and observed several times after dosing and twice daily over a 14-day period for physical condition and mortality.
Type:	oral LD50
Species/Strain:	rat/ MR Wistar
Sex:	male
Number of animals:	20
Vehicle:	water
Year:	1968
GLP:	No. Study conducted prior to GLP/OECD guidelines.
Results:	LD50 = 1000 mg/kg body weight
Remark:	This study is assigned a reliability code of 2e according to the criteria established by Klimisch et al. (1997). It was not conducted under GLP or OECD guidelines but generally meets scientific standards, is well documented and is accepted for assessment.
Summary details:	Ten male rats received 2-(2'-hydroxy-5'-octylphenyl) benzotriazole as a 10% aqueous dispersion at concentrations of 1.25, 2.5, 5.0, and 10 mg/kg. There were no clinical signs of toxicity or mortality in any of the animals. Mean body weight increased throughout the study. All animals survived dosing and there were no abnormal findings upon gross autopsy.
References:	'Acute Oral Toxicity of CL 37,207. American Cyanamid Company, January 2, 1968.

[2] See listing of evaluation codes (Klimisch, H.J., et al.) p. 138

14 GENETIC **TOXICITY IN VIVO**

Test Substance: 2-(2'-hydroxy-5'-octylphenyl) benzotriazole, CAS# 3 147-75-9

No Data Found

15. GENETIC TOXICITY IN VITRO

Test substance: 2-(2'-hydroxy-5'-octylphenyl) benzotriazole, CAS# 3147-75-g

Method: This study was conducted under OECD Guideline 471, Genetic Toxicology: Salmonella typhimurium, Reverse Mutation Assay, May 26, 1983. The chemical was tested for mutagenic effects on histidine -auxotrophic mutants of Salmonella typhimurium: TA 98, TA 100, TA 1535, TA 1537 and in a tryptophan-requiring strain of Escherichia coli: WP2uvrA. The tests were performed with six concentrations of the test substance, a negative and a positive control, with and without microsomal activation. The plates were incubated for about 48 hours at 37 ± 1.5°C in darkness. Thereafter, they were evaluated by counting the number of colonies and determining the background lawn.

Type: Reverse mutation

System of testing: Salmonella typhimurium TA 98, TA 100, TA 1535, TA 1537 and **E.** Coli WP2uvrA.

Concentration: 20.5, 61.7, 185.2, 555.5, 1666.6 and 5000.0 ug / plate

Controls: Solvent alone was used as the negative control.
The positive controls were the following reference mutagens:

A. Experiment without microsomal activation:

Strain	Mutagen	Solvent	Concentration (ug/ plate)
TA 100	sodium azide	bidistilled water	5.0
TA 1535	sodium azude	bidistilled water	5.0
WP2uvrA	4-nitroquinoline-N-oxide	DMSO	2.0
TA 98	2-nitrofluorene	DMSO	20.0
TA 1537	9(5)-aminoacridine	DMSO	150.0

B. Experiment with microsomal activation:

Strain	Mutagen	Solvent	Concentration (ug/ plate)
TA 100	2-aminoanthracene	DMSO	2.5
TA 1535	cyclophosphamide.H2O	bidistilled water	400.0
WP2uvrA	2-aminoanthracene	DMSO	50.0
TA 98	2-aminoanthracene	DMSO	2.5
TA 1537	2-aminoanthracene	DMSO	2.5

GLP: Yes

Year: 1991

Results: In the experiments performed with and without microsomal activation, comparison of the number of histidine- or tryptophan-prototrophic mutants in the controls and after treatment revealed no marked differences.

Table 1. Mean number of revertant colonies from experiments with metabolic activation

	Negative Control	Positive Control (ug/ Plate)	Test substance (ug/ plate) 625.0	1250.0	2500.0	5000.0
TA 100	166.5	1778	161	147	143	128
TA 1535	10.0	1452	8.5	11.0	6.5	6.5
E.coli WP2uvrA	19.5	847.0	13.0	13.5	14.5	18.0
TA 98	20.5	1278.5	15.5	18.5	18.0	8.0
TA 1537	6.5	1491.5	8.0	6.5	7.0	6.0

Table 2. Mean number of revertant colonies from experiments with metabolic activation

	Negative Control	Positive Control (ug/ Plate)	Test substance (ug/ plate) 625.0	1250.0	2500.0	5000.0
TA 100	140.0	1936.0	141.5	123.0	120.0	113.0
TA 1535	12.5	377.0	13.0	13.0	9.0	9.0
E.coli WP2uvrA	22.0	1015.0	23.5	15.0	13.0	15.5
TA 98	40.5	2239.5	31.5	27.5	25.5	30.0
TA 1577	17.5	249.0	12.0	13.0	11.5	7.5

Remarks: This study is assigned a rating code of 2b (Guideline study with acceptable restrictions)

References: Bacterial Mutagenicity Screening Test. CIBA-GEIGY Limited, Basel, Switzerland; Sept. 02, 1991.

16. REPEATED DOSE TOXICITY'

Test Substance:	2-(2'-hydroxy-5'-octylphenyl) benzotriazole, CAS# 3 147-75-9
Method:	30-day Repeated Feeding Study
Species/Strain:	rat/MR Wistar
Sex:	male/female
Route of administration:	oral
Exposure period:	30 days
Frequency of treatment:	Ad lib feeding regimen.
Doses:	0, 1.25, 2.5, and 5 % (corresponding to 0, 1.286, 2.594, and 5.658 g/kg/day) mglkg
Control group:	yes
Year:	1968
GLP:	No. Study conducted prior to GLP/OECD Guidelines.
Results:	NOAEL = 5.658 g/kg body weight
Remark:	This study is assigned a reliability code of 2e according to the criteria established by Klimisch et a/. (1997)'.
Summary details:	A 30-day repeated oral toxicity study with 2-(2'-hydroxy-5'-octylphenyl) benzotriazole was conducted to assess its potential to cause systemic toxicity and adverse effects in the rat. 2-(2'-Hydroxy-5'-octylphenyl) benzotriazole was administered orally to rats (5/sex/group), at concentrations of 0, 1.25, 2.5, and 5 % (0, 1.286, 2.594, and 5.658 g/kg/day) for 30 days. Body weight and food intake were recorded for each animal. At the end of the feeding period, the animals were killed and subjected to a thorough gross autopsy. There were no deaths during the test period, and the overall appearance and behavior of the animals were good. Hydronephrosis, common to this strain of rat, was noted in 4 animals from the 5% group and in 3 controls. However, no lesions were noted which were attributable to ingestion of the test material.

Summary of Results				
Concentration in diet (%)	0	1.25	2.5	5.0
Number of animals (male + female)	5+5	5+5	5+5	5+5
Mean dosage (g/kg/day)	-	1.286	2.594	5.658
Man initial weight (g)	138.5	137.0	139.30	138.8
Mean food intake (g)	599.2	573.9	609.9	628.1
Mean weight gain (g)	106.7	102.6	106.4	111.9
Mean weight adjusted for food intake (g)	107.5	108.7	104.9	106.6

There was no evidence that the feeding of the test material to rats for 30 days at concentrations of 5% of less had any significant effect in on body weight gain of food intake of the animals.

References:

'CL 37,207: A 30-day Oral Feeding Study, American Cyanamid Company, Report 68-1, 1968

[2] See listing of evaluation codes (Klimisch, H.J., et al.) p. 138

17. DEVELOPMENTAL TOXICITY

Test Substance: 2-(2'-hydroxy-5'-octylphenyl) benzotriazole, CAS# 3147-75-g

No Data Found

18. REPRODUCTIVE TOXICITY

Test Substance: 2-(2'-hydroxy-5'-octylphenyl) benzotriazole, CAS# 3147-75-9

No Data Found

Review of Test Data and Robust Summaries for

2-(2'-Hydroxy-3,5-di-tert-amylphenyl) benzotriazole

CAS No. 25973-55-l

CONTENTS

SUMMARY TABLE

CAS No. 25973-55-l	DATE	RESULTS	FULFILLS REQUIREMENT
PHYSICAL/CHEMICAL ELEMENTS			
Melting Point	2000	80 - 83 °C (measured)	Yes
Boiling Point	2000	477.84 °C (*)	Yes
Vapor Pressure	2000	1.93 x 10^{-10} mm Hg (*)	Yes
Partition Coefficient	2000	log Pow = 7.3 (*)	Yes
Water Solubility	1997	0.015 mg/L @ 25 °C (*)	Yes
ENVIRONMENTAL FATE AND PATHWAYS ELEMENTS			
Photodegradation	2000	Rate Constant: 15.76 x 10^{-12} cm ^{3}/ molecule-set Half-life : 8.14 h (*)	Yes
Stability in Water	2000	This program cannot estimate a hydrolysis rate for this type of structure.	No
Fugacity (*)	2000	Predicted distribution using Level III fugacity model Air 0.000227 % Water 2.16% Soil 40.4 % Sediment 57.5 %	Yes
Biodegradation	1997	Not biodegradable (measured) 10 mg/L: 8% after 28 days 20 mg/L: 2% after 28 days	Yes
ECOTOXICITY ELEMENTS			
Acute Toxicity to Fish	1997	Zebra fish (Brachydanio rerio): LC_{50} (24 – 96 h) => 100 mg/L NOEC = 100 mg/L	Yes
Toxicity to Aquatic Plants	1997	Green algae (Scenedesmus subspicatus): EC_{50} (0 – 72 h) > 10 mg/L	Yes
Acute Toxicity to Aquatic Invertebrates	1997	Daphnia magna: EC_0 (24 h) = 58 mg/L EC_{50} (24 h) > 100 mg/L	Yes

* Estimated Value using EPJWJN Model (Syracuse Research Corporation, 2000)

SUMMARY TABLE (CONTINUED)

CAS No. 25973-55-l	**DATE**	**RESULTS**	**FULFILLS REQUIREMENT**
HEALTH ELEMENTS			
Acute Toxicity	1993	Rat: LD_{50} (Oral) > 2325 mg/kg	Yes
Genetic Toxicity in vivo		No data available	No
Genetic Toxicity in vitro	1979	Non mutagenic	Yes
Repeated Dose Toxicity	1968 1970	Rat : NOEL = 100 ppm dietary Dog : NOEL < 15 mg/kg	Yes
Reproductive Toxicity		No data available	No
Developmental Toxicity/Teratogenicity		No data available	No

1. MELTING POINT

Test substance:	2-(2'-Hydroxy-3,5-di-tert-amylphenyl) benzotriazole CAS No. 25973-55-l
Method:	from Sigma-Aldrich'
GLP:	No
Year:	2001
Results:	80 to 83 °C
Remarks:	The melting point is assigned a reliability code of 2g[2] (data from handbook or collection of data). This value is similar to data reported on the Ciba MSDS of 80 to 88 °C.
References:	[1] www.Sigma-Aldrich.com [2] See listing of evaluation codes (Klimisch, H.J., et al.) p. 138

2. BOILING POINT

Test substance:	2-(2'-Hydroxy-3,5-di-tert-amylphenyl) benzotriazole CAS No. 25973-55-I
Method:	Estimated by the MPBPWIN Program (v. 1.40)' using the adapted Stein and Brown method.
GLP:	No
Year:	2000
Results:	477.84 °C
Remarks:	The boiling point calculation by an accepted method is assigned a reliability code of 2f.
References:	'Syracuse Research Corporation, Syracuse, NY Pollution Prevention (P2) Assessment Framework, U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics (Draft), 1998

3. VAPOR PRESSURE

Test substance:	2-(2'-Hydroxy-3,5-di-tert-amylphenyl) benzotriazole CAS No. 25973-55-I
Method:	Estimated by the MPBPWIN Program (v. 1.28),[1] using the modified Grain method.
GLP:	No
Year:	2000
Results:	1.93×10^{-10} mm Hg
Remarks:	The vapor pressure calculation by an accepted method is assigned a reliability code of 2f. The Ciba MSDS reported a vapor pressure of 4.7×10^{-6} mm Hg but the method was not reported; in the absence of this information the calculated value is used.
References:	'Syracuse Research Corporation, Syracuse, NY Pollution Prevention (P2) Assessment Framework, U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics (Draft), 1998

4. PARTITION COEFFICIENT

Test substance:	2-(2'-Hydroxy-3,5-di-tert-amylphenyl) benzotriazole CAS No. 25973-55-l
Method:	KOWWIN Program (VI .66)
GLP:	No
Year:	2000
Results:	Log Kow = 7.25
Remarks:	The partition coefficient calculation by an accepted method is assigned a reliability code of 2f. The Ciba MSDS reported a log Kow of > 6 but the method was not reported; in the absence of this information the calculated value is used.
References:	'Syracuse Research Corporation, Syracuse, NY Pollution Prevention (P2) Assessment Framework, U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics (Draft), 1998

5. WATER SOLUBILITY

Test substance:	2-(2'-Hydroxy-3,5-di-tert-amylphenyl) benzotriazole CAS No. 25973-55-I
Method:	WSKOW v1.37[1]
Temperature:	**25** °C
GLP:	**No**
Year:	**2000**
Results:	Water solubility = 0.015 mg/L @ 25 °C
Remarks:	The water solubility calculated by an accepted method is assigned a reliability code of 2f. The Ciba MSDS reported a water solubility of <0.01% at 20 °C (< 100 mg/L) but the method was not reported; in the absence of this information the calculated value is used.
References:	'Syracuse Research Corporation, Syracuse, NY Pollution Prevention (P2) Assessment Framework, U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics (Draft), 1998

6. PHOTODEGRADATION

Test substance:	2-(2'-Hydroxy-3,5-di-tert-amylphenyl) benzotriazole CAS No. 25973-55-l
Method:	Estimated by the AOP program (v. 1.87),[1] which estimates rate constants and half-lives of atmospheric reactions of organic compounds with hydroxyl radicals and ozone in the atmosphere.
GLP:	No
Year:	**2000**
Results:	For reaction with hydroxyl radicals, the predicted half-life of the chemical is rapid.
Rate constant:	15.76 x 10^{-12} cm^3/molecule-sec Half-life: 8.14 h
Remarks:	The photodegradation calculation by an accepted method is assigned a reliability code of 2f.
References:	'Syracuse Research Corporation, Syracuse, NY Pollution Prevention (P2) Assessment Framework, U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics (Draft), 1998

7. STABILITY IN WATER

Test substance:	2-(2'-Hydroxy-3,5-di-tert-amylphenyl) benzotriazole CAS No. 25973-55-l
Method:	Estimated by the HYDROWIN Program (v. 1.64).[1]
GLP:	No
Year:	**2000**
Results:	This program could not estimate a hydrolysis rate for this type of structure.
Remarks:	The stability in water will be determined for representative compounds from this category at a later time.
References:	'Syracuse Research Corporation, Syracuse, NY Pollution Prevention (P2) Assessment Framework, U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics (Draft), 1998

a. THEORETICAL DISTRIBUTION (FUGACITY CALCULATION)

Test substance:	2-(2'-Hydroxy-3,5-di-tert-amylphenyl) benzotriazole CAS No. 25973-55-l
Method:	EPI WIN level III Fugacity model.
Year:	2000
GLP:	No
Results:	Distribution using level III fugacity model

Air	0.000227 %
Water	2.16%
Soil	40.4 %
Sediment	57.5 %

Remarks:	The fugacity calculation by an accepted method is assigned a reliability code of 2f.
References:	'Syracuse Research Corporation, Syracuse, NY Pollution Prevention (P2) Assessment Framework, U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics (Draft), 1998

9. BIODEGRADATION

Test substance:	2-(2'-Hydroxy-3,5-di-tert-amylphenyl) benzotriazole CAS No. 25973-55-I Batch No. EN 135146.82
Method:	OECD Guideline 301 B. Bacteria collected from activated sludge of the sewage treatment plant of CH - 4153 Reinach on 20/09/88. The preparation was carried out according to the method described in the guideline, with the exception that the volume of test solution was reduced from 3 to 1.5L
Test Type:	Aerobic
Inoculum:	Fresh sewage treatment plant sample (per guideline)
Concentration:	Reference substance: Aniline, Merck No.: 1261, 20 mg/ L Test substance: 10 mg/ L and 20 mg/ L
Medium:	Sewage sludge (per guideline)
GLP:	No
Year:	1988
Results:	Biodegradation Reference substance: 20 mg/L: 94.4 % after 28 days. Test substance : 10 mg/L: 8 % after 28 days 20 mg/L: 2 % after 28 days Under the test conditions, no biodegradation was observed.
Conclusion:	Substance is not biodegradable according to OECD definition.
Remarks:	The study is assigned a reliability code of 2b (Guideline study with acceptable restrictions).
Reference:	Report on the Test for Ready Biodegradability of Tinuvin 328 in the Modified Sturm Test, OECD-GUIDELINE No. 301 B (Paris 1981), Dr. A. de Morsier, 01/11/88, CIBA - GEIGY Ltd., Basle, Switzerland.

10. ACUTE TOXICITY TO FISH

Test substance:	2-(2'-Hydroxy-3,5-di-tert-amylphenyl) benzotriazole CAS No. 25973-55-I Batch No. EN 135146.82
Method:	OECD Guideline No. 203 (Paris 1984). This study was performed as a limit test with a concentration of 100 mg/L (nominal),
Type of test:	Static
Species:	Zebra Fish (Brachydanio rerio)
Supplier:	West-Aquarium, D-3422 Bad Lauterberg
Length:	24 mm (19-27 mm)
Weight:	0.12 g (0.05-0.17 g)
Loading:	0.08 g/L
Exposure period:	96 h
Analytical monitoring:	No. Testing based on nominal concentrations.
GLP:	No
Year:	1988
Results:	LC_{50} (96 h) > 100 mg/L NOEC = 100 mg/L A limit test was performed with 20 fish (10 per aquarium) exposed to the test compound and 10 control fish. No mortality occurred throughout the test. A precipitate indicated the solubility limit was exceeded.
Remarks:	This study is assigned a reliability code of 2b (Guideline study witjh acceptable restrictions) according the criteria established by Klimisch *et al* (1997).
Reference:	Report on the test for acute toxicity of TK 10046 to Zebra Fish, OECD-Guideline No. 203, Paris 1984, Project No. 884368; Dr. A. de Morsier, 1 0/10/88, Ciba-Geigy Limited, Basel, Switzerland.

11. TOXICITY TO AQUATIC PLANTS

Test substance:	2-(2'-Hydroxy-3,5-di-tert-amylphenyl) benzotriazole CAS No. 25973-55-I Batch No. EN 169792.24; purity: 99%
Method:	The protocol generally followed OECD 201, algae growth inhibition test. Tests were conducted in 250-mL Erlenmeyer flasks containing 100 mL of solution. Each test level and control was prepared in triplicate.
Species:	Green algae *(Scenedesmus subspicatus)*
Endpoint:	Growth rate
Exposure period:	72 h
Initial Cell Density:	10^4 cells/mL
Test Concentrations:	0.10, 1.0, and IO mg/L plus control (0.0) and vehicle blank (acetone). Concentrations were mixed separately and sonicated for 15 minutes initially and for 30 minutes after stocks were brought to final volumes with media containing algae nutrient. Each flask was inoculated with approximately 1 .O x 10^4 cells/ml. Cell counts were made at 0 and 72 hours.
Vehicle:	Acetone
Analytical monitoring:	**No** Testing based on nominal concentrations.
GLP:	No. The study generally followed good laboratory practices, however, the in-life portion was not audited.
Year:	1993
Results:	EC_{50} (0 - 72 h) > IO mg/L Total Loading. After 72 hours, cell counts were 61%, 80% and 74% of controls for the 0.1, 1 .0 and 10.0 mg/L levels, respectively. A precipitate in the 10 mg/L level suggested that the solubility limit was exceeded.
Remarks:	This study is assigned a reliability code of 2C (comparable to guideline study with acceptable restrictions) according the criteria established by Klimisch et *al* (1997). The data indicate that even if with solubility enhanced by using acetone as a carrier, a concentration high enough to inhibit ceil growth 50% can not be reached in water.
Reference:	Acute Toxicity Screen of Tinuvin 328 to *Scenedesmus subspicatus*; Stephen L. Hicks, Douglas W. Gledhill; ABC Laboratories, Inc., Environmental Toxicity, 7200 E. ABC Lane, Columbia. Missouri; Final Report # 40855.

12. ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Test substance:	2-(2'-Hydroxy-3,5-di-tert-amylphenyl) benzotriazole CAS No. 25973-55-I Batch No. 135146.82
Method:	OECD Guideline No. 202 (Paris 1984).
Type of test:	Static
Species:	Daphnia magna Straus 1820
Exposure period:	24 hours
Analytical monitoring:	No. Testing based on nominal concentrations.
GLP:	No
Year:	1988
Results:	EC_{50} (24 h) > 100 mg/L EC,, (24 h) = 58 mg/L Daphnia exposed to concentrations of 5.8, 10, 18, 32, and 58 mg/L showed no effects. Two of ten daphnia were immobilized at 100 mg/L. A slight precipitate at all levels showed the water solubility limit was exceeded.
Remarks:	The study is assigned a reliability code of 2C (comparable to guideline study with acceptable restrictions).
Reference:	Report: Test for acute Toxicity of TK 10046 to Daphnia magna; OECD-Guideline No. 202, Paris 1984; Project No.: 884369; Drs. A. De Morsier, H. Rufli; CIBA- GEIGY Ltd., Basle, Switzerland.

13. ACUTE ORAL TOXICITY

Test substance:	2-(2'-Hydroxy-3,5-di-tert-amylphenyl) benzotriazole CAS No. 25973-55-l Batch No. EN 2299
Method:	The chemical was suspended with polyethylene glycol (PEG 400), and homogeneously mixed. Tif : RAIF (SPF) rats were kept at room temperature ($22 \pm 1\ ^0C$) and on a 10 hour light-cycle day. They received ad libitum food and water. Prior to treatment animals were adapted to laboratory for a minimum of 4 days. The body weights ranged from 160 to 180 grams. During the treatment and observation period the animals were housed in groups of 5 in Macrolon cages. Animals fasted overnight were treated by oral intubation.
Species/strain:	Tif : RAIf (SPF) strain
Sex:	Males / Females
No. Animals/Group:	**5** each /sex/dose level
Doses:	1392, 1800, 2325 mg/ kg test-substance-basis (4640, 6000, 7750 mg / kg dosing solution - 30% a.i.)
Post dosing observation period:	**14** days
GLP:	No
Year:	1978
Results:	Oral LD_{50} > 2325 mg/ kg TK 10046. Within 2 hours after treatment the rats in all dosage groups showed sedation, dyspnea, curved position and ruffled fur. Animals recovered within 8 to 9 days. No deaths occurred during the 14-day observation period. Necropsy showed no gross organ changes.
Remarks:	The study is assigned an acceptability code of 2C (comparable to guideline study with acceptable restrictions).
Reference:	Acute Oral LD_{50} In The Rat Of TK 10046; CIBA-GEIGY Ltd. Toxicology/ Pathology, Project-no. Siss 6481. January 23, 1978.

14. GENETIC TOXICITY IN VIVO

Test substance: 2-(2'-Hydroxy-3,5-di-tert-amylphenyl) benzotriazole
CAS No. 25973-55-l

No Data found

15. GENETIC TOXICITY IN VITRO

Test substance:	2-(2'-Hydroxy-3,5-di-tert-amylphenyl) benzotriazole CAS No. 25973-55-l Batch No. EN 2299
Method:	This study was not conducted under OECD guidelines, but was conducted using the methods described by Ames et. a/. (1973, 1975). The chemical was tested for mutagenic effects on histidine-auxotrophic mutants of Salmonella typhimurium: TA 98, TA 100, TA 1535 and TA 1537. The investigations were performed with the following concentrations of the test substance with and without microsomal activation: 25, 75, 225, 675 and 2025 ug/ 0.1 ml.
Type:	Bacterial mutagenicity
GLP:	**No**
Year:	1979
Results	In the experiments performed with and without microsomal activation, comparison of the number of back-mutant colonies in the controls and the cultures treated with the various concentrations of the test chemical revealed no marked deviations. No evidence of point mutations was detected.
Remarks:	This study is assigned a rating code of 2c (comparable to guideline study with acceptable restrictions).
References:	Salmonella/ Mammalian - Microsome Mutagenicvity Test With TK 10046. (Test for mutagenic properties in bacteria); CIBA-GEIGY Limited, Basel,, Switzerland; November 6, 1979. 'Ames, B.N., Lee, F.D., and Durston, W.E., "An improved bacterial test system for the detection and classification of mutagens and carcinogens, Proc. Natl. Acad. Sci. USA, 70, 782-786, 1973. [3]Ames, B.N., Durston, W.E., Yamasaki, E., and Lee, F.D., "Carcinogens are mutagens: a simple test system combining liver homogenates for activation and bacteria for detection," Proc. Natl. Acad. Sci. USA, 70, 2281-2285, 1973. [4]Ames, B.N., McCann, J., and Yamasaki, E., "Methods for detecting carcinogens and mutagens with the Salmonella/mammalian-microsome mutagenicity test, Mutat. Res., 31, 347-364, 1975.

16. REPEATED DOSE TOXICITY

Two studies fulfill this requirement.

A 90-Day Sub-chronic Study in the Rat

Test substance:	2-(2'-Hydroxy-3,5-di-tert-amylphenyl) benzotriazole CAS No. 25973-55-l
Method:	Although this study was not formally conducted under OECD guidelines, the method parallels OECD Guideline 409 "Sub-chronic Oral Toxicity – Non-Rodent: 90-Day study". Female and male albino rats were fed with a diet containing 0, 100, 200, 400, 800 and 1600 ppm for 90 days.
Species/strain:	Albino rats, (derived from the Wistar strain)
Age at initiation:	Newly weaned rats
Average body weight	43- 56 g
Sex:	Male/Female
No. animals/group:	10 / sex / treatment level
Route of administration:	Incorporated into the diet
Exposure period:	7 days per week, 3 months.
Frequency of treatment:	Daily
Dose:	0, 100, 200, 400, 800 and 1600 ppm.
Control group:	Concurrent (diet without admixing the test article)
GLP:	No
Year:	*1968*
Results:	NOEL: < 100 ppm NOAEL: 100 ppm ~ 22 mg/ kg bw / day No mortality occurred. Body weight gain and food consumption were reduced in the highest dose group. Hematological analysis revealed a treatment-related decrease of hemoglobin content and packed cell volume in males at 200 ppm and above. In females, this effect was less pronounced. The data from clinical chemistry revealed an increase of glucose-6-phosphatase at lower dose groups with a steady-state level at about 200 ppm. The liver, kidney, spleen and testes weights were increased. There was also some hints for increased thyroid weights in the higher dose groups. The liver was identified as the main target organ in gross and histopathological investigations: a greenish-drab discoloration was observed in males and also in females at

	the higher dose levels. Microscopic examination revealed occasionally foci of necrosis and a slight proliferation of bile duct epithelia. Parenchymal cells were enlarged. In the kidney tubular necrosis was observed in some males from the higher feeding levels. In females, a treatment-related, yellowish-brown pigmentation in the cytoplasm of the proximal tubular cells was noted. From the observations made, the NOEL was found to be < 100 ppm. The NOAEL showing no adverse toxic blood, liver or kidney effects is estimated to be at 100 ppm.
Remarks:	This study is assigned a reliability code of 2c (comparable to guideline study with acceptable restrictions) according to the guidelines described by Klimisch et *al* (1997).
Reference:	Short-Term (49-Day) and Subchronic (90-Day) Toxicity Studies with RY 1137 in Rats. Central Institute for Nutrition and Food Research, Zeist, The Netherlands; Report No. R2640. March 1968.

B. 90-Day Study in the Beagle Dog:

Test substance:	2-(2'-Hydroxy-3,5-di-tert-amylphenyl) benzotriazole CAS No. 25973-55-l
Method:	Although this study was not formally conducted under OECD guidelines, the method parallels OECD Guideline 409 "Subchronic Oral Toxicity – Non-Rodent: 90-Day study". A total of 20 female and 20 male Beagle dogs were fed with a diet containing 0, 15, 30, 60, 120 and 240 mg/kg body weight for 3 months.
Species/strain:	Beagle Dogs, registered by the American Kennel Club, New York (USA)
Age at initiation:	Mean Age: male dogs 35 weeks female dogs 32 weeks Mean weiaht: male dogs 11.5 kg female dogs 8.1 kg
Sex:	Male/Female
No. animals/group:	3 / sex / each chemical treatment level 5 / sex in control group.
Route of administration:	Incorporated into the diet
Exposure period:	7 days per week, 3 months.
Frequency of treatment:	Daily
Dose:	15, 30, 60, 120, 240 mg/ kg body weight.
Control group:	Concurrent (diet without admixing the test article)
GLP:	**No**
Year:	1970
Results:	NOEL: > 15 mg/ kg bw One male from the high dose group died on the 8th week of treatment. Toxicity was more pronounced in the males than in the females. Body weight loss and depression of food consumption occurred in the high dose group. Ophthalmology revealed no findings. Hematological analysis revealed signs of anemia at the two highest dose groups. The data from blood chemistry revealed slight increased bilirubin, GTP, GOT and alkaline phosphatase activity in the serum. Gross-and histopathological investigation showed increased liver weights associated with severe liver damage including icterus (jaundice) in a few dogs in the 120 and 240 mg / kg groups. Microscopic changes included fatty degeneration of hepatocytes, protein

globules in the cytoplasm, kupffer cell hyperplasia and centrolobular choleostasis. The kidneys were also exhibited toxicity. In some animals of the higher dose roups, atrophy of the uterus, abnormal spermiogenesis, and atrophy of the prostate were observed. From the observations made, the NOEL was found to be < 15 mg/kg body weight with liver as the most sensitive organ.

Remarks: This study is assigned a reliability code of 2c (comparable to guideline study with acceptable restrictions) according to the guidelines described by Klimisch et *al* (1997).

Reference: Report (A 0176/049): Three-Months Toxicity Study, TINUVIN 328, Dietary Administration - Beagle Dogs, institute for Industrielle und Siologische Forschung, Koln, Den; Project-no. A 01761049. May 20, 1970.

17. REPRODUCTIVE TOXICITY

Test substance: 2-(2'-Hydroxy-3,5-di-tert-amylphenyl) benzotriazole
CAS No. 25973-55-l

No Data found

18. DEVELOPMENTAL TOXICITY/ TERATOGENICITY

Test substance: 2-(2'-Hydroxy-3,5-di-tert-amylphenyl) benzotriazole
CAS No. 25973-55-l

No Data found

Review of Test Data and Robust Summaries for

2-(2H -Benzotriazol-2-yl)-4,6-bis(1 -methyl-l -phenylethyl) phenol

CAS No. 70321-86-7

CONTENTS

SUMMARY TABLE

CAS No. 70321-86-7			
PHYSICAL/CHEMICAL ELEMENTS	**DATE**	**RESULTS**	**FULFILLS REQUIREMENT**
Melting Point	2000	139 - 143 °C (measured)	Yes
Boiling Point	2000	599.75 °C (*)	Yes
Vapour Pressure	2000	1.62×10^{-14} mm Hg (*)	Yes
Partition Coefficient	1984	log P = > 6.5 (measured)	Yes
Partition Coefficient	2000	log P = 7.21 (*)	Yes
Water Solubility		< 0.04 mg/L (measured)	Yes
Water Solubility	2000	0.01 mg/L (*)	Yes
ENVIRONMENTAL FATE AND PATHWAYS ELEMENTS			
Photodegradation	2000	For reaction with hydroxyl radical, predicted rate constant = 121×10^{-12} cm^3/molecule-sec predicted half-life = 1.06 h (*)	Yes
Stability in Water	2000	This program cannot estimate a hydrolysis rate for this type of structure.	No
Fugacity (*)	2000	Predicted distribution using Level III fugacity model Air 0.00 % Water 2.19 % Soil 40.1 % Sediment 57.7 %	Yes
Biodegradation	1984	Not readily biodegradable (measured) 20 mg/ L - 99% in 28 days	Yes
ECOTOXICITY ELEMENTS			
Acute Toxicity to Fish	1984	Zebra fish (Brachydanio rerio): LC_{50} (96 h) > 67 mg/L	Yes
Toxicity to Aquatic Plants	1993	Scenedesmus subspicatus EC_{50} (72 h) > 100 mg/L	Yes
Acute Toxicity to Aquatic Invertebrates	1984	Daphnia magna straus 1820 EC_0 (24 h) > 91 mg/L EC_{50} (24 h) > 91 mg/L	Yes

* Estimated Value using EPIWIN Model (Syracuse Research Corporation, 2000)

SUMMARY TABLE (CONTINUED)

CAS No 70321-86-7 *HEALTH ELEMENTS*	DATE	RESULTS	FULFILLS REQUIREMENT
Acute Toxicity	1978	Rat: LD_{50} (Oral) > 7750 mg/kg	Yes
	1993	Rat: LD_{50} (dermal) > 2000 mg/kg	Yes
Genetic Toxicity in vivo:			
A: Nucleus Anomaly Test	1985	Chinese hamster: Nonmutagenic in somatic (bone marrow) mutation assay (exposed by gavage 1250, 2500, or 5000 mg/kg/day for 2 days)	Yes
B: Chromosomal Aberration	1985	Chinese hamster: Sister Chromatid Exchange, Bone marrow. No significant increase of the number of SCE was found.	Yes
Genetic Toxicity in vitro:			
A: Reverse mutation	1982	Salmonella typhimurium: No increase in mutations with or without metabolic activation	Yes
B: Autoradiographic DNA repair test	19x4	Tif:RAIf (SPF) male rat hepatocytes: No evidence of induction of DNA damage by test substance or by its metabolites.	Yes
Repeated Dose Toxicity	1987	Albino rats 90-day ,Dietary NOEL = 50 ppm.	Yes
Reproductive Toxicity		No data available	No
Developmental Toxicity/Teratogenicity	1987	No embyotoxic activity and teratogenic potency was observed following the oral administration of daily doses of 300, 1000, and 3000 mg/ kg	Yes

1. MELTING POINT

Test substance:	2-(2H-Benzotriazol-2-yl)-4,6-bis(1-methyl-1-phenylethyl) phenol CAS No. 70321-86-7
Method:	From Sigma-Aldrich'
GLP:	No
Year:	2001
Results:	139 - 143°C
Remarks:	The melting point was obtained from Sigma-Aldrich MSDS, and was assigned a reliability code of 2g (data from handbook or collection of data).* The MSDS from Ciba Specialty Chemicals Corp reported a similar melting point range of 135 ▪ 143 °C.
References:	[1]www.sigma-aldrich.com [2]See listing of evaluation codes (Klimisch, H.J., et al.) p. 138

2. BOILING POINT

Test substance:	2-(2H-Benzotriazol-2-yl)-4,6-bis(1-methyl-1-phenylethyl) phenol CAS No. 70321-86-7
Method:	Estimated by the MPBPWIN Program (v. 1.4)[1,2], using the adapted Stein and Brown method.
GLP:	No
Year:	2000
Results:	*599.75* °C
Remarks:	In the absence of reliable experimental data, the boiling point was calculated using an accepted method and assigned a reliability code of 2f [3].
References:	'Syracuse Research Corporation, Syracuse, NY. 'Pollution Prevention (P2) Assessment Framework, U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics (Draft), 1998. [3]See listing of evaluation codes (Klimisch, H.J., et al.) p. 138

3. VAPOR PRESSURE

Test substance:	2-(2H-Benzotriazol-2-yl)-4,6-bis(1-methyl-1-phenylethyl) phenol CAS No. 70321-86-7
Method:	Estimated by the MPBPWIN Program (v. 1.40)[1,2] , using the modified Grain method.
GLP:	No
Year:	2000
Results:	1.62×10^{-14} mm Hg
Remarks:	In the absence of reliable experimental data, the vapor pressure was calculated by an accepted method and assigned a reliability code of 2f[3].
References:	'[1]Syracuse Research Corporation, Syracuse, NY. '[2]Pollution Prevention (P2) Assessment Framework, U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics (Draft), 1998. [3]See listing of evaluation codes (Klimisch, H.J., et al.) p. 138

4. PARTITION COEFFICIENT

Test substance:	2-(2H-Benzotriazol-2-yl)-4,6-bis(1-methyl-1-phenylethyl) phenol CAS No. 70321-86-7
Method:	OECD Guideline for Testing of Chemicals No.107 "Partition Coefficient (n-octanol / water)" and EEC annex V TG A 3.8, "Partition Coefficient".
GLP:	Yes
Temperature:	**25** °C
Year:	**1984**
Results:	Log Pow = 6.5
Remarks:	The partition coefficient value of 6.5 was calculated by fragment method (EEC A 3.8) [1]. This study was assigned a reliability code of 1 (reliable without restriction) as it was conducted under relevant guidelines.*
References:	'"Report on Partition Coefficient", Ciba Geigy Ltd., Basel, Switzerland. Dr. P. Moser, 12/03/84. [2]See listing of evaluation codes (Klimisch, H.J., et al.) p. 138

5. WATER SOLUBILITY

Test substance:	2-(2H-Benzotriazol-2-yl)-4,6-bis(1-methyl-1-phenylethyl) phenol CAS No. 70321-86-7
Method:	OECD Guideline 105.
Temperature:	20 °C
GLP:	Yes
Year:	**1985**
Results:	Water solubility @ 20 °C is < 0.04 mg/L
Remarks:	This study was assigned a reliability code of 1 (reliable without restriction) as it was conducted under relevant guidelines.* The value calculated by the EPIWIN model is 0.01 mg/L.
References:	'Report on Water Solubility, Ciba-Geigy Limited, Basel, Switzerland, 1985 [2]See listing of evaluation codes (Klimisch, H.J., et al.) p. 138

6. PHOTODEGRADATION

Test substance:	2-(2H-Benzotriazol-2-yl)-4,6-bis(I-methyl-I-phenylethyl) phenol CAS No. 70321-86-7
Method:	Estimated by the AOP program (v. 1.87)[1,2], which estimates rate constants and half-lives of atmospheric reactions of organic compounds with hydroxyl radicals and ozone in the atmosphere.
GLP:	No
Year:	**2000**
Results:	For reaction with hydroxyl radicals, the predicted half-life of the chemical is rapid. Rate constant: 120.78 x 10^{-12} cm^3/molecule-sec Half-life: 1.06 h
Remarks:	There is no reliable experimental data. The photodegradation calculation by an accepted method is assigned a reliability code of 2f [3].
References:	'Syracuse Research Corporation, Syracuse, NY *Pollution Prevention (P2) Assessment Framework, U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics (Draft), 1998. [3]See listing of evaluation codes (Klimisch, H.J., et al.) p. 138

7. STABILITY IN WATER

Test substance:	2-(2H-Benzotriazol-2-yl)-4,6-bis(1-methyl-1-phenylethyl) phenol CAS No. 70321-86-7
Method:	Estimated by the HYDROWIN Program (v. 1.67).[1,2]
GLP:	No
Year:	**2000**
Results:	No estimate available.
Remarks:	This program could not estimate a hydrolysis rate for this type of structure.
References:	'Syracuse Research Corporation, Syracuse, NY [2]Pollution Prevention (P2) Assessment Framework, U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics (Draft), 1998.

8 THEORETICAL DISTRIBUTION (FUGACITY CALCULATION)

Test substance: 2-(2H-Benzotriazol-2-yl)-4,6-bis(1-methyl-1-phenylethyl) phenol
CAS No. 70321-86-7

Method: EPI WIN level III Fugacity model. [1,2]

Year: 2000

GLP: No

Results: Distribution using level III fugacity model

Air	0.00 %
Water	2.19 %
Soil	40.1 %
Sediment	57.7 %

Remarks: The fugacity was calculated using an accepted method and assigned a reliability code of 2f [3].

References: ‘Syracuse Research Corporation, Syracuse, NY.

*Pollution Prevention (P2) Assessment Framework, U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics (Draft), 1998.

[3]See listing of evaluation codes (Klimisch, H.J., et al.) p. 138

9. **BIODEGRADATION**

Test substance:	2-(2H-Benzotriazol-2-yl)-4,6-bis(1-methyl-1-phenylethyl) phenol CAS No. 70321-86-7 Batch No. EN 02885.32
Method:	The protocol generally followed OECD Guideline 301 B, Ready Biodegradability: Modified Sturm Test. The only deviation from the test guideline is the volume of the test solution was reduced from 3.0 L to 1.5 L. Bacteria was collected from activated sludge of the sewage treatment plant.
Test System:	Bacteria collected from a sewage treatment plant.
Duration:	28 days
Temperature:	22 ± 2^0 c
Reference Substance:	Aniline MERCK No.:1261
Concentrations:	Reference substance: 20 mg/ L Test substance: 10 mg/ L, and 20 mg/ L.
GLP:	**Yes**
Year:	**1984**
Results:	The biodegradation for test substance was calculated as: 10 mg/L - 6 % in 28 days 20 mg/L - 3 % in 28 days The biodegradation for the reference substance was calculated as: 20 mg/L - 99% in 28 days
Conclusion:	Substance is not biodegradable according to OECD definition.
Remarks:	This study is assigned a reliability code of 1 as it was conducted under OECD and GLP Guidelines.*
Reference:	Report On The Test For Biodegradability OF TK 12443 In The Modified Sturm Test (OECD-Guideline No. 301 B, Paris 1981); (1984), Dr. A. De Morsier; Ciba-Geigy Ltd. Basle, Switzerland. [2]See listing of evaluation codes (Klimisch, H.J., et al.) p. 138

10. ACUTE TOXICITY TO FISH

Test substance:	2-(2H-Benzotriazol-2-yl)-4,6-bis(1 -methyl-l -phenylethyl) phenol CAS No. 70321-86-7 Batch No. EN 02885.32
Method:	OECD Guideline No. 203 (Paris 1981). Glass aquaria of 20 L (filled with 15 L) were used. Water source was dechlorinated tap water (carbon filter) with 178 mg $CaCO_3$/ L hardness. There were 10 fish per concentration and control and 10 fish per aquarium. Tests were conducted in duplicate. This study was performed as a limit test with a concentration of 100 mg/L (nominal). Highest vehicle concentration was 891 mg/L.
Type of Test:	Static
Species:	Zebra Fish (Brachydanio rerio)
Supplier:	West-Aquarium, D-3422 Bad Lauterberg
Length:	25 mm (22-28 mm)
Weight:	0.14g (0.05 - 0.19 g)
Loading:	0.09 g/L
Test Concentration:	100 mg/L (nominal), 67 mg/L (actual)
Controls:	Vehicle: 887 mg tetrahydrofuran, 4 mg ARKOPAL N150 per liter water. Blank: Water
Exposure period:	96 h
Analytical monitoring:	**No**
GLP:	**No**
Year:	**1984**
Results:	There were no mortalities in control or treated groups. LC_{50} (24 h): > 67 mg/L LC_{50} (48 h): > 67 mg/L LC_{50} (72 h): > 67 mg/L LC_{50} (96 h): > 67 mg/L

Table 1 : Analytical data of test concentrations

Nominal Concentration mg/L	Measured Concentrations 0 h mg/L	96 h mg/L
100	73	59
100	67	67

Remarks: This study is assigned a reliability code of 2b (guideline study with acceptable restrictions) according the criteria established by Klimisch et *a/* (1997), as it was conducted under OECD Guidelines'.

Reference: 'Report On The Test For Acute Toxicity Of TK 12443 To Zebra Fish; Project No.: 84 09 01; Drs K. Mueller, A. De Morsier; Ciba-Geigy Ltd. Basle, Switzerland.

[2]See listing of evaluation codes (Klimisch, H.J., et al.) p. 138

11. TOXICITY TO AQUATIC PLANTS

Test substance:	2-(2H-Benzotriazol-2-yl)-4,6-bis(1-methyl-1-phenylethyl) phenol CAS No. 70321-86-7 Batch No. EN 306296.12
Method:	The static Scenedesmus subspicatus toxicity screen was conducted in 250-mL Erlenmeyer flasks containing 100 mL of algae nutrient media or test solution. Each test level and the controls were prepared in triplicate. The water quality parameters of temperature and pH were measured in each test solution at test initiation. The temperature for all the test solutions was 23 ^{0}C and the pH ranged from 7.4 to 7.6. Algal cell counts were conducted at 0 hour in the control and vehicle blank replicates and in all test chambers after 72 hours.
Species:	Green Algae (Scenedesmus subspicatus)
Test Procedure:	Static
Age of Culture at Study Initiation:	3 days old
Test concentration :	1 .0, 10, and 100 mg/L (nominal)
Vehicle:	Dimethylformamide (DMF)
Exposure period:	72 h
Analytical monitoring:	Yes
GLP:	Yes
Year:	1993
Results:	EC_{50} (O-72 h) > 100 mg/L NOEC (O-72 h) = 100 mg/L
Remarks:	This study is assigned a reliability code of 2C (comparable to guideline study with acceptable restrictions) according the criteria established by Klimisch et al (1997) [2].
Reference:	Acute Toxicity Screen Of Tinuvin 900 to Scenedesmus subspicatus; Final Report # 40858; (1993), Stephen L. Hicks, Douglas W. Gledhill; Performing Laboratory: ABC Laboratories, Inc. Columbia, Missouri 65202; Sponsor: Ciba-Geigy, Ltd., Additives Division, AD 1.21, Basel, Switzerland.

[2] See listing of evaluation codes (Klimisch, H.J., et al.) p. 138

12. ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Test substance:	2-(2H-Benzotriazol-2-yl)-4,6-bis(1-methyl-1-phenylethyl) phenol CAS No. 70321-86-7 Batch No. 135146.82
Method:	OECD Guideline No. 202 (Paris 1981). Reconstituted water was prepared by dissolving 65 mg $NaHCO_3$, 274 mg $CaCl_2$ (2 H_2O), 123 mg $MgSO_4$ (7 H_2O), 6 mg KCI in 1 liter of bidistilled water. Total hardness was 240 mg $CaCO_3$/L; temperature was 20 $\pm$ 1 °C. 20 daphnia/conc and control. (4 replicates of 5 daphnia) were taken. Initially the test substance appeared homgeneously distributed. Slight precipitation occurred after 24 h at concentrations > 18 mg/L nominal. Samples for analysis were taken after 0 h and 24 h exposure.
Type of test:	Static
Species:	Daphnia magna Straus 1820
Exposure period:	24 hours
Test Concentration:	10, 18, 32, 58, and 100 mg/L (nominal) 6.0, 9.6, 20.5, 27.2, 91.2 mg/L (actual)
Controls:	Vehicle: 887 mg tetrahydrofuran; 4 mg ARKOPAL N150 per liter water. Blank: Water.
Analytical monitoring:	Yes.
GLP:	No.
Year:	1984
Results:	EC-Values (24 hour) graphically determined: EC_{50} (24 h) : > 91 mg/L EC,, (24h) : > 91 mg/L EC_{100} (24h) : > 91 mg/L Controls: Immobilization blank 0 % Immobilization vehicle 0 % Values are based on actual initial concentrations. The test substance precipitated immediately at concentrations > 100 mg/L (nominal).

Table 1 : Analytical data of test concentrations

Nominal Concentration mg/L	Measured Concentrations Oh 96 h mg/L	mg/L
10	6.0	3.0
18	9.6	4.0
32	20.5	7.8
100	11.1	11.1

Remarks: The study is assigned a reliability code of 2C (comparable to guideline study with acceptance restrictions) according the criteria established by Klimisch et *al* **(1997).** [2]

Reference: Report On The Test For Acute Toxicity of TK 12443 To Daphnia Magna; OECE-Guideline No. 202, Paris 1984; Project No.: 84 09 00; Drs. A. de Morsier, H. Rufli, K. Mueller; CIBA-GEIGY Ltd., Basel, Switzerland.

[2] See listing of evaluation codes (Klimisch, H.J., et al.) p. 138

13 ACUTE TOXICITY

Several studies were conducted to assess the acute toxicity. The oral study is selected for evaluation of this endpoint.

A. ORAL

Test substance:	2-(2H-Benzotriazol-2-yl)-4,6-bis(1-methyl-1-phenylethyl) phenol CAS No. 70321-86-7 Batch No. A 16-234/5
Method:	Test material was suspended in polyethylene glycol (PEG 400), and homogeneously mixed. Tif: RAIF (SPF) rats were kept at room temperature of 22 ± 1 ^{0}C, at a relative humidity of 55 ± 5 % and on a 10 hours light cycle day. They received ad libitum rat food and water. The body weight ranged from 160 to 180 grams. During the treatment and observation period the animals were housed in groups of 5 in Macrolon cages. Animals fasted overnight were treated by oral intubation. Physical condition and rate of deaths were monitored throughout the whole observation period.
Species/strain:	Tif: RAIF (SPF) strain (healthy bred rats-7 to 8 weeks old)
Sex:	Males/Females
No. Animals/Group:	5 each/dose level
Doses:	1000, 2150, 4640, 7750 mg/kg
Vehicle:	Polyethylene glycol (PEG 400)
Post dosing observation period:	14 days
GLP:	No
Year:	1978
Results:	Within 2 hours after treatment the rats in all dosage groups showed sedation, dyspnoea, curved position and ruffled fur. Sedation became more accentuated as the dose was increased. Animals recovered within 8 to 10 days and were submitted to a necropsy at the end of observation period. Necropsies showed no substance related gross organ changes. The acute oral LD50 in rats of both sexes observed over a period of 14 days is > 7750 mg/kg. The test material has therefore practically no acute toxicity to the rat by this route of administration.
Remarks:	The study is assigned a reliability code of 2b (guideline study with acceptance restrictions) according the criteria established by Klimisch et *a/* (1997). This study was not conducted under GLP or OECD guidelines. [2]

Reference:

Report On Acute Oral LD_{50} In The Rat Of TK 12443; CIBA_GEIGY Ltd. Basle, Switzerland; Project No. 784965; Drs. Med. Vet. R. Bathe, med. Vet. K. Sachasse, December 21, 1978.

[2]See listing of evaluation codes (Klimisch, H.J., et al.) p. 138

B. DERMAL

Test substance:	2-(2H-Benzotriazol-2-yl)-4,6-bis(1-methyl-1-phenylethyl) phenol CAS No. 70321-86-7 Batch No. EN 306296.12
Method:	The study design followed OECD Guideline 402; 92/69/EEC, B.3., "Acute Dermal Toxicity", adopted February 24, 1987. The test material was evenly dispersed on the skin of albino rats (1 O/group). It was covered with a gauze-lined semi-occlusive dressing fastened around the trunk with an adhesive elastic bandage. After 24 hours the dressing was removed and the skin was cleaned with lukewarm water. Thereafter the skin reaction was appraised repeatedly.
Species/strain:	Albino rats
Initial Body Weight Range:	212 to 237 g
Dose level:	2000 mg/kg body weight
Total number of animals:	10 rats (5 males and 5 females)
Frequency of application:	One dose
Exposure period:	24 hours
Post exposure observation period:	14 days
Vehicle:	0.5% (w/v) Carboxymethylcellulose in 0.1% (w/v) aqueous polysorbate 80.
GLP:	**Yes**
Year:	**1993**
Results:	LD50 in rats of both sexes > 2000 mg/kg body weight. Piloerection was seen, being a common symptom in acute dermal tests. The animals recovered within 1 day. No mortalities occurred during this study. Necropsy examination did not reveal any gross pathologic alterations.
Remarks:	This study is assigned a reliability code of 2e (meets generally accepted scientific standards, well documented and acceptable for assessment).*
Reference:	"Acute Dermal Toxicity Study In The Rat", Test No. 934003, TK 12443 (Tinuvin 900) Report; April 7, 1993: Dr. Phil. H. R. Hartman; Ciba-Geigy Limited, Additives Division, 4002 Basel, Switzerland. [2]See listing of evaluation codes (Klimisch, H.J., et al.) p. 138

14. GENETIC TOXICITY IN VIVO

A. NUCLEUS ANOMALY

Test Substance:	2-(2H-Benzotriazol-2-yl)-4,6-bis(1-methyl-1-phenylethyl) phenol CAS No. 70321-86-7 Batch No. **EN 02885.32**
Method:	This study was not conducted under OECD or GLP guidelines. Chinese hamsters of either sex were used for the tolerability and mutagenicity tests. The animals were kept at 23-24 ^{0}C and a relative humidity of 5657%. The room was illuminated for 12 hours daily. In the tolerability test the animals were treated with a single dose of 5000 mglkg body weight. In the mutagenicity test, animals were gavaged with 1250, 2500 or 5000 mglkg test material in 20 mL/kg 0.5% CMC solution, positive control, cyclophosphamide (128 mglkg in 20 mL/kg 0.5% CMC solution), or negative control (20 mL/ kg of 0.5% CMC). Treatment consisted of daily application on 2 consecutive days, Twenty-four hours after the second application, animals were sacrificed and bone marrow was harvested from the shaft of both femurs. Bone marrow cells were examined.
Type:	Nucleus anomaly test.
Species/strain:	Chinese hamster
Sex:	Male/Female
No. Animals/group:	Tolerability test: 2 males and 2 females Mutagenicity test: 6 males and 6 females.
Route of administration:	Gavage.
Exposure period:	**2** days
Doses:	1250, 2500 and 5000 mglkg per day
Vehicle:	0.5% carboxymethylcellulose (20 mL /kg)
Controls:	Concurrent Positive: 128 mg/kg cyclophosphamide Negative: Vehicle only (0.5% aqueous solution of sodium carboxymethyl cellulose)
GLP:	No
Year:	**1985**
Results:	In all dosage groups the percentage of cells displaying anomalies of nuclei did not differ significantly from the negative control. The test material is considered to be non-mutagenic.

Table 1 Percent of cells with anomalies of nuclei

Dose	Animal No.	% Cells with Anomalies of Nuclei
Control	1	0.0
(0.5% CMC)	2	0.1
	3	0.1
		0.0
		0.0
		0.0
Cyclophosphamide		9.3
(128 mg/kg)	2	8.1
	3	5.1
	4	1 1 9
	5	9.8
	6	12.3
1250 mg/kg	1	0.1
	2	0.0
	3	0.1
	4	0.0
	5	0.1
	6	0.0
2500 mg/kg	1	0.3
	2	0.1
	3	0.1
		0.2
	5	0.0
	6	0.0
5000 mg/kg	1	0.2
	2	0.2
	3	0.0
	4	0.0
	5	0.0
	6	0.0

The data represent the sum of single Jolly bodies, fragments of nuclei in erythrocytes, micronuclei in erythroblasts, micronuclei in leucopoietic cells, bizarre forms of nuclei, and polyploid cells. The study reported separate incidences for each endpoint, but only the total is represented.

Remarks: Although not conducted under GLP or OECD guidelines, this study meets generally accepted scientific standards, is well documented, and is acceptable for assessment (reliability code 2e). The findings are consistent with those of other in vitro and in vivo studies for this chemical.'

Reference: '"Nucleus Anomaly Test on Somatic Interphase Nuclei of Chinese Hamster (Test for Mutagenic Effects on Bone Marrow Cells)", Ciba Geigy, Limited, Basel-Switzerland. Dr. D. Miiller, 02/11/85.

[2]See listing of evaluation codes (Klimisch, H.J., et al.) p. 138

B. SISTER CHROMATID EXCHANGE

Test Material:	2-(2H-Benzotriazol-2-yl)-4,6-bis(1-methyl-1-phenylethyl) phenol CAS No. 70321-86-7 Batch No. EN 02885.32
Method:	This study was not conducted under OECD or GLP guidelines. Chinese hamsters of either sex were used for the tolerability and mutagenicity tests. The animals were kept at 23-24 ^{0}C and a relative humidity of 56-57%. The room was illuminated for 12 hours daily. In the tolerability test the animals were treated with single dose of 5000 mglkg body weight. In the mutagenicity test, animals were gavaged with 1250, 2500 or 5000 mg/kg test material in 20 mL/kg 0.5% CMC solution, positive control, 7,12-dimethylbenzanthracene (DMBA) (100 mg/kg in 20 mL/kg 0.5% CMC solution), or negative control (20 mL/ kg of 0.5% CMC). Chinese hamsters were administered the test compound by gavage, and sacrificed 24 h after the exposure and 2 h after an i.p. injection of colcemide. From the bone marrow, drop-preparations were made and stained according to a modified fluorochrome plus Giemsa technique (Perry and Wolf, 1974 [2]. Goto et *al,* 1978 [3]; Allen *et al,* 1977 [4]). Slides were scored for the number of sister chromatid exchanges (Perry and Evans, 1975 [5]).
Type:	Sister chromatid exchange, bone marrow
Species/strain:	Chinese hamsters (Cricetulus griseus)
Sex:	Male/Female
No. Animals/Group:	In the tolerability test: 2 males and 2 females, In the mutagenicity test: 4 males and 4 females.
Route of Administration:	Gavage
Exposure period:	24 hours
Doses:	1250, 2500 and 5000 mg/kg
Controls:	Positive control: 7,12-Dimethylbenzanthracene (DMBA) in 20 mL/kg 0.5% aqueous solution sodium carboxymethylcellulose Negative control: 20 mL/kg 0.5% aqueous solution sodium carboxymethylcellulose
GLP:	No, but was subjected to periodic quality assurance evaluation'.
Year:	1985
Results:	In the various dose groups no significant increase of the number of sister chromatid exchange's (SCE) was found in comparison with the negative control. The positive control group showed a highly significant increase of SCE's per cell (5.96) in comparison with the negative control (3.15) SCE's/ cell.

Table 1. The Effect of Test material and Positive control on Bone Marrow Cells of Chinese Hamster

Dose	Animal No.	Mean Value of SCEs per cell per animal	Mean Value of SCEs per cell per group
Control	1	3.80	
(0.5% CMC)	2	2.84	
		2.96	
	4	3.00	3.15
DMBA	1	5.36	
(100 mg/kg)	2	5.72	
	3	5.88	
	4	6.88	5.96
1250 mg/kg	1	3.24	
	2	3.32	
		3.44	
	4	2.76	3.19
2500 mglkg	1	3.04	
	2	2.44	
	3	2.68	
	4	4.00	3.04
5000 mg/kg	1	3.64	
	2	3.68	
	3	3.28	
	4	2.88	3.37

Remarks: Although not conducted under GLP or OECD guidelines, this study does meet generally accepted scientific standards, is well documented, and is acceptable for assessment (reliability code 2e).[6] The findings of this study are consistent with those of other in vitro and in vivo studies for this chemical.

Reference:

'Sister Chromatid Exchange Studies On Somatic Cells Of Chinese Hamsters; Test No: 840859; Ciba Geigy, Limited, Basel, Switzerland; March 21, 1985.

*PERRY, P. and S. WOLFF: New Giemsa Method for the Differential Staining of Sister Chromatids. Nature 251, 156-158 (1974).

[3]GOTO, K., S. MAEDA, Y. KANO and T. SUGIYAMA: Factors Involved in Differential Giemsa-Staining of Sister Chromatids. Chromosoma (Berl.) 66, 351-359 (1978).

[4]ALLEN, J.W., C.F. SHULER, R.W. MENDES and S.A. LATT: A Simplified Technique for in vivo Analysis of Sister Chromatid Exchanges Using 5-Bromodeoxyuridine Tablets. Cytogenet. Cell Genet. 18, 231-237 (1977).

[5]PERRY, P., and H.J. EVANS: Cytological Detection of Mutagen-Carcinogen Exposure by Sister Chromatid Exchange. Nature 258, 121-125 (1' 975).

"See listing of evaluation codes (Klimisch, H.J., et al.) p. 138

15. GENETIC TOXICITY IN VITRO

A. REVERSE MUTATION

Test substance:	2-(2H-Benzotriazol-2-yl)-4,6-bis(1-methyl-1-phenylethyl) phenol CAS No. 70321-86-7 Batch No. EN 24375
Method:	This study was not conducted under OECD guidelines, but was conducted using the methods described by Ames et al (1973, 1975)[2-4]. This chemical was tested for mutagenic effects on histidine -auxotrophic mutants of Salmonella typhimurium: TA 98, TA 100, TA 1535, TA 1537. The tests were performed with the following concentrations of the trial substance with and without microsomal activation: 25, 75,225, 675 and 2025 ug IO.1 ml. Each Petri dish contained: 1) approx. 20 mL of minimum agar, plus salts and glucose, 2) 0.1 mL of the solution of the test substance or the vehicle and 0.1 mL of a bacterial culture (in nutrient broth, 0.8% plus 0.5% NaCl) in 2.0 mL of soft agar. The soft agar was composed of: 100 mL of 0.6% agar solution with 0.6% NaCl and 10 mL of a solution of I-histidine, 0.5 mM and +biotin 0.5 mM. In the experiments in which the substance was metabolically activated, 0.5 mL of an activation mixture was also added. 1 mL activation mixture contained: 0.3 mL S9 fraction of liver from rats induced with Aroclor 1254 and 0.7 mL of a solution of co-factors.
Type:	Reverse mutation
System of testing:	Salmonella typhimurium TA 98, TA 100, TA 1535, TA 1537
Concentration:	25, 75, 225, 675 and 2025 ug 10.1 ml.
Controls:	Acetone alone was used for the negative control. Positive control experiments were carried out simultaneously with the following substances: 1) for strain TA 98: daunorubitin-HCI, 5 and 10 pg / 0.1 mL phosphate buffer 2) for strain TA 100: 4-nitroquinoline-N-oxide, 0.125 and 0.25 ug / 0.1 mL phosphate buffer; 3) for strain TA 1535: N-methyl-N'- nitro-N-nitrosoguanidine, 3 and 5 pg / 0.1 mL phosphate buffer: 4) for strain TA 1537: 9(5)aminoacridine hydrochloride monohydrate, 50 and 100 pg / 0.1 mL DMSO.
GLP:	No
Year:	1982
Results:	In the experiments performed with and without microsomal activation, comparison of the number of histidine-prototrophic mutants in the controls and after treatment with the test substance revealed no marked differences.

Table 1. Mean number of revertant colonies from experiments without metabolic activation

	TA 98	TA 100	TA 1535	TA 1537
Control	29	104	17	5
25 µg/0.1 mL	23	101	16	6
75 µg/0.1 mL	30	117	13	8
225 µg/0.1 mL	33	104	18	12
675 µg/0.1 mL	32	107	21	9
2025 µg/0.1 mL	33	111	17	4

Table 2. Mean number of revertant colonies from experiments with metabolic activation (without/with pre-incubation)

	TA 98	TA 100	TA 1535	TA 1537
Control	49	93	11	8
25 µg/0.1 mL	50	100	12	6
75 µg/0.1 mL	50	103	19	5
225 µg/0.1 mL	55	98	21	6
675 µg/0.1 mL	50	96	22	6
2025 µg/0.1 mL	64	103	20	5

Remarks: This study is assigned a rating code of 2e (meets generally accepted scientific standards, well documented and accepted for assessment).[5]

References:

'Salmonella/Mammalian-Microsome Mutagenicity Test With TK 12443. (Test for mutagenic properties in bacteria): CIBA-GEIGY Limited, Basel, Switzerland; February 5, 1982.

[2]Ames, B.N., Lee, F.D., and Durston, W.E., "An improved bacterial test system for the detection and classification of mutagens and carcinogens, Proc. Natl. Acad. Sci. USA, 70, 782-786, 1973.

[3]Ames, B.N., Durston, W.E., Yamasaki, E., and Lee, F.D., "Carcinogens are mutagens: a simple test system combining liver homogenates for activation and bacteria for detection," Proc. Natl. Acad. Sci. USA, 70, 2281-2285, 1973.

[4]Ames, B.N., McCann, J., and Yamasaki, E., "Methods for detecting carcinogens and mutagens with the Salmonella/mammalian-microsome mutagenicity test, Mutat. Res., 31, 347-364, 1975.

[5]See listing of evaluation codes (Klimisch, H.J., et al.) p. 138

B. DNA REPAIR TEST

Test substance:	2-(2H-Benzotriazol-2-yl)-4,6-bis(1-methyl-1-phenylethyl) phenol CAS No. 70321-86-7
Method:	Freshly isolated hepatocytes from a male rat (Tif. RAlf (SPF),weight: 215 g) were cultivated in Williams' medium containing 10% foetal bovine serum. Based on the results of a toxicity test, the highest testable concentration was 50 ug/ml. From each of the treatment groups and from the positive and the negative controls 150 nuclei in altogether three slides (50 cells/ slide) were scored.
Type:	Autoradiographic DNA repair test on rat hepatocytes.
Species/strain:	Tif:RAlf (SPF) male rats
Sex:	Male
Vehicle:	Acetone (Merck)
Positive Control:	DMN (100mM)
Concentration:	50, 10, 2 and 0.4 ug/ ml medium
No. of cultures per group:	*4*
Year:	**1984**
Results:	In the experiments performed, comparison of the mean number of silver grains per nucleus in the negative controls and in the cultures treated with various concentrations of the test substance revealed no marked deviations. It is concluded that, there is no evidence of induction of DNA damage by the test substance or its metabolites.
Remarks:	The study was assigned a reliability code of 2 (valid with restriction).[2]
Reference:	'Autoradiographic DNA Repair Test On Rat Hepatocytes; 11/28/84, Dr. E. Puri, Dr. D. Muller, Ciba-Geigy Limited, Basel, Switzerland.

[2] See listing of evaluation codes (Klimisch, H.J., et al.) p. 138

16. REPEATED DOSE TOXICITY

Test substance:	2-(2H-Benzotriazol-2-yl)-4,6-bis(1-methyl-1-phenylethyl) phenol CAS No. 70321-86-7 Project No.: 840860 Batch No. EN 02885.32
Method:	This study was conducted under OECD guideline for testing of chemicals, subchronic oral Toxicity-Rodent: 90 day study, No. 408, adopted May 12, 1981. This toxicity study was conducted in order to determine the potential oral toxicity of the test article upon continuous administration in feed for 3 months and to estimate a no-observable effect level of exposure. The experiment was carried out under specified pathogen free standard laboratory conditions. The temperature was maintained at 22± 2 ^{0}C, relative humidity of 55 ± IO % and 12 hour light per day was used.
Species/strain:	Albino Rats, Tif: RAIF (SPF), hybrid of RII l/if x RII 2/Tif
Age at initiation:	approximately 4 weeks at delivery
	Mean weiaht:
	males: 64-96 g
	females: 63 ▪ 86 g
Sex:	Male/Female
No. animals/group:	20 males and females per dose group
Route of admininstration:	Dietary, Incorporated into the diet
Exposure period:	92-94 days
Frequency of treatment:	Daily
Dose:	0, 50, 300, 2000, and 10,000 ppm
GLP:	Yes.
Year:	1987
Results:	No treatment related clinical symptoms and no signs of systemic toxicity were observed during the study. No death occurred during the course of study. No evidence of a reaction to the treatment was observed in: eyes, hearing, body- weight, hematological investigations, blood chemistry, urine analysis and macroscopical findings. A statistically significant increase in mean liver weight, in liver to body and/or liver to brain ratios was observed in males and females from group 5 (10,000 ppm) and 4 (2,000 ppm), and in females from group 3 (300 ppm).

A slight to moderate hypertrophy and/or cytoplasmic vacuolization of hepatocytes were observed in males and females of group 5 (10,000 ppm) and 4 (2,000 ppm), and in females group 3 (300 ppm). A NOEL was set at 50 ppm.

MEAN ORGAN WEIGHTS (G) AND RATIOS (PERCENTAGE OF BODY AND BRAIN WEIGHT)

ORGANS	DOSE IN PPM								
	0		300		2000		10000		TREND
	NO	MEAN	NO	MEAN	NO	MEAN	NO	MEAN	
BODY	10	209.890	10	228.290	10	223.570"	10	229.370*	
BRAIN	10	2.076	10	2.060	10	2.087	10	2.085	
BRAIN / BODY	10	0.991	10	0.904*	10	0.937	10	0.913*	
LIVER	10	8.339	10	11.838*	10	11.569*	10	11.456*	→
LIVER/ BODY	10	3.973	10	5.180	10	5.165*	10	5.011*	→
LIVER/BRAIN	10	401.698	10	575.907*	10	558.229*	550.089*		→
KIDNEYS	10	1.996	10	1.965	10	1.830	10	1.990	
KIDNEYS BODY	10	0.949	10	0.861*	10	0.820*	10	0.873*	
KIDNEYS /BRAIN	10	96.212	10	95.538	10	88.048	10	95.915	
ADRENALS	10	0.087	IO	0.087	IO	0.089	10	0.092	
ADRENALS/BODY	10	0.0417	10	0.0383	10	0.0400	10	0.0405	
ADRENALS/BRAIN	10	4.195	10	4.249	10	4.254	10	4.430	

* indicates difference (location and/or dispersion) between control (group 1) and group x

→ indicates positive trend from control to highest dosage group

Remarks: This study is assigned a reliability code of 1 (reliable without restriction) according to the guidelines described by Klimisch *et a/* (1997). [2]

Reference: "Final Report, TK 12443 ▪ Three-Month Oral Toxicity Study In Rats (Administration In Feed)"; GU Project No. 840860, 01/22/87, Dr. Phil II W. Basler, Dr. Med. Vet. W. Gfeller, Ciba -Geigy Limited, Basel, Switzerland.

[2] See listing of evaluation codes (Klimisch, H.J., et al.) p. 138

17. REPRODUCTIVE TOXICITY

Test substance: 2-(2H-Benzotriazol-2-yl)-4,6-bis(1 -methyl-l -phenylethyl) phenol
CAS No. 70321-86-7

No data available

18. DEVELOPMENT TOXICITY/TERATOGENICITY

TERATOGENICITY IN RATS

Test substance:	2-(2H-Benzotriazol-2-yl)-4,6-bis(1-methyl-1-phenylethyl) phenol CAS No. 70321-86-7
Method:	The study followed OECD Guideline for testing of chemicals, "Teratogenicity" no. 414, adopted May 12, 1981. In this study the chemical was evaluated for possible embryotoxic activity and teratogenic potency in rats. Female rats were mated overnight with males of proven fertility in a ratio of one male to three females. The day on which spermatozoa were found in the vaginal smear was designated as Day 0 of pregnancy. Throughout the experiment, successfully mated females were housed in groups of 4 in an air-conditioned room at a temperature of 21 ± 1 °C and a humidity of 55% ± 15%. The room was illuminated for 12 hours daily. Animals were provided standard diet and tap water ad libitum. The compound was administered by oral gavage on Days 6 through 15 of pregnancy. During the treatment, general condition, weight gain, food consumption, and symptoms were checked daily. The females were killed a short time prior to expected delivery and subjected to macroscopic pathological examination. The uteri were dissected and contents examined. Live fetuses were weighed, sexed and evaluated for external, visceral and/or skeletal abnormalities.
Species/strain:	Albino Rats, Tif: RAIF (SPF), hybrids of RII/ lx RII/2
Sex:	Female
Initial mean body weight of females: 180 - 200 g	
Initial age of females:	about 2 months
Route of administration:	Gavage
Duration of the test:	10 days
Exposure period:	Days 6 through 15 of gestation
Frequency of treatment:	Daily
Doses:	0,300, 1000 and 3000 mg/kg of body weight
Control group:	Yes; Concurrent vehicle
GLP:	Yes
Year:	1987
Results:	Maternal data: The body-weight gain and food consumption was comparable for all 3 dose groups. No clinical signs or symptoms were recorded. A few animals from control and treatment groups developed

necrotic areas on the skin which were not considered to be relatied to the chemical treatment. No spontaneous deaths were observed.

Pregnancy rates were comparable for all groups (92 – 100%). No differences in embryo or fetal mortality were observed.

Fetal data: On the comparison of the group means of body weights, a significant reduction was recorded for the 1000 mg/kg group. Also an increased delay of skeletal maturation was found for this dose group. In the absence of effects in the high dose group thiese effects were considered incidental to treatment.

The external examination of the live fetuses revealed two malformations:

- a fetus of the control group showed generalized edema
- a fetus of the high-dose group showed an *omphalocele.* *

*Omphalocele is the failure of ventral closure during late stages of embryonic development.

Conclusions: The compound did not exhibit either a teratogenic or an embryotoxic effect under the conditions of this experiment.

Remarks: This study was assigned a reliability code of 2b (guideline study with acceptance restrictions). It was conducted under OECD guidelines and the methods employed are standard techniques.'

Reference: 'Final Report ▪ TK 12443, Teratology Study In Rats, GU Project No. 840862; Dr. H. Fritz, 12103187; Ciba Geigy Limited, Basel, Switzerland.

[2]See listing of evaluation codes (Klimisch, H.J., et al.) p. 138

GENERAL REFERENCE

Klimisch, H.J., Andreae, M and Tillman, U. A *systemic approach for evaluating the quality of experimental toxicological and ecotoxicological data. Regulatory Toxicology and Pharmacology. 25: I-5, 1997*

1 = Valid without restriction
1 a: GLP guideline study
1 b: Comparable to guideline study
Ic: Meets national standard methods (AFNOR/DIN)
Id: Meets generally accepted scientific standards and is described in sufficient detail

2 = Valid with restriction
2a: Guideline study without detailed documentation
2b: Guideline study with acceptance restrictions
2c: Comparable to guideline study with acceptable restrictions
2d: Meets national standard methods with acceptable restrictions
2e: Meets generally accepted scientific standards, well documented and acceptable for assessment
2f: Accepted calculation method
2g: data from Handbook or collection of data

3 = Invalid
3a: Documentation insufficient for assessment
3b: Significant methodological deficiencies
3c: Unsuitable test system

4 = Not assignable
4a: Abstract
4b: Secondary literature
4c: Original reference not yet available
4d: Original reference in a foreign language
4e: Documentation insufficient for assessment